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# INDEX

## TO

# The New England Journal of Medicine

## Volume 234, January 3, 1946 to June 27, 1946

### PAGES ACCORDING TO WEEKLY ISSUES

Pages	No	Date	Pages	No	Date
1-36	1	Jan 3	459-490	14	Apr 4
37-70	2	Jan 10	491-518	15	Apr 11
71-102	3	Jan 17	519-544	16	Apr 18
103-136	4	Jan 24	545-572	17	Apr 25
137-168	5	Jan 31	573-616	18	May 2
169-205	6	Feb 7	617-654	19	May 9
207-240	7	Feb 14	655-682	20	May 16
241-278	8	Feb 21	683-712	21	May 23
279-312	9	Feb 28	713-748	22	May 30
313-356	10	Mar 7	749-772	23	June 6
357-392	11	Mar 14	773-808	24	June 13
393-426	12	Mar 21	809-848	25	June 20
427-458	13	Mar 28	849-878	26	June 27

### BOOK REVIEWERS

Abbott, John A	Freedman, Harold J	Phaneuf, Louis E
Augustine, Donald L	Goldberg, Bernard I	Pope, Alton S
Ballard, James F	Goodale, Robert L	Quigley, Thomas B
Barton, Robert B	Green, Robert M	Rackemann, Francis M
Belding, David L	Kazanjian, Varaztad H	Reggio, A William
Brodny, M Leopold	Kelemen, George	Resnik, Joseph
Brown, Ethan A	Kuhns, John G	Robey, William H
Brues, Austin M	Lahey, Frank H	Root, Howard F
Buck, Robert W	Lane, C Guy	Savitz, Harry A
Castleman, Benjamin	Larson, Carroll B	Schadt, George L
Chute, Richard	Leary, Timothy	Segal, Maurice S
Cohen, Mandel E	Lever, Walter F	Shattuck, George C
Colby, Fletcher H	Lippman, Fritz	Smith, George G
Daland, Ernest M	Lombard, Herbert L	Smith, Richard M
Dameshek, William	Lowry, Franklin P	Sosman, Merrill C
Dearborn, Lester W	Mansfield, James S	Spector, Benjamin
Dodge, Carroll V	McCarthy, Francis P	Starr, Arnold
Downing, John G	Meigs, Joe V	Stone, Moses J
Eades, M Fletcher	Meltzer, Philip E	Viets, Henry R
Edwards, Edward A	Morrison, Hyman	Waite, J Herbert
Farber, Sidney	Moses, Sanford H	Walker, Burnham S
Faulkner, James M	Mueller, S Richard	Wesselhoeft, Conrad
Faxon, Nathaniel W	Myerson, Abraham	Wheeler, Ralph E
Fine, Jacob	Nye, Robert N	White, Franklin W
Finland, Maxwell	O'Hara, Dwight	White, Paul D
Fitz, Reginald	Osgood, Robert B	Wiggin, Sidney C
	Paine, David	

### KEY TO ABBREVIATIONS

c — correspondence  
 cr — case record  
 e — editorial  
 mdph — Massachusetts Department of Public Health

mms — Massachusetts Medical Society  
 mp — medical progress  
 misc — miscellany  
 mr — meeting report

n — notice  
 o — obituary  
 \* — original article

## SUBJECT INDEX

## A

- ABDOMEN [Allen] 408 - mp  
     [Dunphy & others] 545\*  
 ABDOMINAL surgery [Allen] 408 - mp  
     wounds, postoperative care [Dunphy & others] 545\*  
 ABSCESSSES multiple [Miller & others] 508 - cr  
 ACNE treatment [Stevens] 100 - c  
 ACTINOMYCOSIS [Allen & others] 870 - cr  
     [Miller & others] 508 - cr  
 ADENOCARCINOMA [Bartlett & others] 161 - cr  
     [Simeone] 344 - cr  
 ADOLESCENCE [Stuart] 666, 693, 732 - mp  
 AGRANULOCYTOSIS [McManus] 17\*  
 AINNUM [Tye] 152\*  
 AMERICAN ASSOCIATION OF OBSTETRICIANS, Gynecologists  
     and Abdominal Surgeons Foundation, prize contest  
     168 - n  
 AMERICAN ASSOCIATION FOR STUDY OF GOITER, June 20-22,  
     312 - n  
 AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, May 6-  
     11 458 - n  
 AMERICAN BOARD OF OPHTHALMOLOGY 277 - misc  
 AMERICAN COLLEGE OF CHEST PHYSICIANS, June 29 544 - n  
 AMERICAN COLLEGE OF SURGEONS 135 - misc  
 AMERICAN COMMITTEE FOR YUGOSLAV RELIEF [Schick &  
     others] 876 - c  
 AMERICAN CONGRESS OF PHYSICAL MEDICINE, Sept 4-7  
     616 - n  
 AMERICAN MEDICAL ASSOCIATION 424 - c  
 AMPULLA of Vater [Bartlett & others] 161 - cr  
     [Richardson] 482 - cr  
 ANEMIA [Fienberg & Quigley] 527\*  
     hemolytic [Ginsberg] 826\*  
 ANESTHESIA at McGill 277 - misc  
     spinal complications [Lium] 691\*  
 ANEURYSM [Boyd] 370\*  
     [Brailey & others] 449 - cr  
     coarctation [Friedenberg & Sokol] 552\*  
     rupture [Moritz & others] 270 - cr  
     stenosis [Palmer] 272 - cr  
     ventricular [Penner & Peters] 523\*  
 ANGINA PECTORIS, treatment [Stearns & others] 578\*  
 ANNOUNCEMENTS  
     Abkowitz, Herbert 391  
     Abramson, Julius 518  
     Adams, F Denette 278  
     Albright, Hollis L 102  
     Alexander, Leo 136  
     Babb, Warren D 772  
     Babson, William W 356  
     Balboni, Victor G 772  
     Balch, Franklin G, Jr 878  
     Barker, Robert H 278  
     Barr, Joseph S 312  
     Beigelman Herman 682  
     Berezin, Martin A 278  
     Bolan, Samuel 772  
     Brines, William S 772  
     Buddington, Weston T 312  
     Burrage, Walter S 391  
     Capodiceci, F H 572  
     Cary, Francis F 878  
     Cass, Leo J 572  
     Cataldo, Robert J 544  
     Cincotti, John J 102  
     Cohen, Benjamin 458  
     Corkery, James R 356  
     Cutler, Joseph G 136  
     Dalrymple, Sidney C 772  
     Denny, George P 772  
     Derow, Sidney 356  
     Drooker, J Charles 278  
     Dunphy, J Englebert 518  
     Edwards, Edward A 616  
     Eley, R Cannon 458  
     Factor, Joseph 682  
     Famighetti, Joseph A 682  
     Faulkner, James M 458  
     Faunce, Calvin B 458  
     Flake, Carlyle G 36  
     Foster, Sawyer 168  
     Franssen, Clifford C 356  
     Frothingham, Channing 772  
     Gahm, Irvin G 356  
     Gardner, Stuart N 356  
     Gauld, A Gordon 356  
     Gillespie Luke 772  
     Glendy, R Earle 206  
     Glicklich, Earl A 392  
     Glickman, Alfred M 772  
     Goodwin, Robert H 278  
     Gorman, Richard J 356  
     Gosman, George H R 518  
     Gregg, Ward I 278  
     Gundersen, Trygve 544  
     Hahn, Joseph 458  
     Halsted, James A 70  
     Harken, D E 392  
     Harrington, Philip V 391  
     Harrison, James 878  
     Hearne, Thomas M 278  
     Hermanson, Louis 712  
     Hoerr, Stanley O 518  
     Horne, Elwood O 772  
     Hoyt, Lyman H 356  
     Hudson, Henry W 518  
     Jacobson, Bernard M 518  
     Jaffee, I H 278  
     Joel Samuel W 356  
     Johnson, Allen S 278  
     Joplin, Robert J 102  
     Kimball, Stanley 70  
     Kontoff, Henry A 36  
     Ladd, William C 356  
     Lanigan, William N 356  
     Levenson, Walter S 36  
     Levine, Samuel 458  
     Lewis, Elihu I 518  
     Liebman, Sumner D 544  
     Lund, Charles C 356  
     Lynch, J P 392  
     Mabrey, Roy E 682  
     Macaluso, A 878  
     Maltby, George L 654  
     Marcus, Philip S 654  
     Marka, George A 168  
     Martin, S Forrest 312  
     McCarthy, Charles J 356  
     Michelsen, Jost J 102  
     Moses, Edward T 168  
     Murphy, John A 712  
     Nadel, Frederick P 712  
     Norton, Hermon 391  
     Palmer, Robert S 102  
     Parsons, Langdon 206  
     Pilcher, Lewis S 572  
     Pollock, Henry M, Jr 458  
     Prather, George C 572  
     Pratt, Theodore C 102  
     Regan, James J 278  
     Scazzello, N S 458  
     Scelso Salvatore 102  
     Schlosberg, Charles 772  
     Shaw, Jules H 168  
     Shinberg, John D 356  
     Shuman, H Herman 654  
     Sprague, Howard B 168  
     Staffier, D Thomas 458  
     Stein, Calvert 392  
     Strieder, John W 392  
     Sullivan, Garrett L 654  
     Swan, Channing S 312, 392  
     Swan, Charles L, Jr 392  
     Swartz, Jacob H 392  
     Taylor, Grantley W 102

Tiede, Joseph W 518  
 Van Raalte, Leslie H 772  
 Viets, Henry R 278  
 Volk, Ralph 168  
 Walsh, Francis X 70  
 Weiss, L Robert 616  
 Wells, Ralph H 616  
 Wetherbee, Winthrop, Jr 102  
 Wolbarsht, Abraham 36  
 Zetzel, Louis 682  
 Zonis, Jonathan 458

ANTISEPTIC solution new [Brown & others] 468\*  
 AORTA, aneurysm [Bland & others] 196 - cr  
 APPLICANTS 351 - mms  
 ARTHRITIS Bacterial [Hirsh & others] 853\*  
 ASCORBIC, acid [Holmes & others] 47\*  
 ASTHMA, bronchial [Greene] 639 - cr  
 ATROPINE poisoning [Alexander & others] 258\*

## B

BACTERIOLOGY, laboratories [Bailey] 682 - c  
 (HENRY JACOB) BIGELOW MEDAL (See Notes) 682 - misc  
 (HERMANN M.) BIGGS MEMORIAL LECTURE, April 4, 206  
 BLOOD donors, syncope [Moloney & others] 114\*  
 BLUE TRIANGLE 68 - mms  
 BOARDS of health, trends [Hilliard] 391 - c  
 BONE, diseases [Fienberg & Quigley] 527\*  
 BOOK REVIEWS  
     *American Red Cross First Aid Textbook* 772  
     *Clinical Roentgenology of Digestive Tract* [Feldman] 655  
     *Diagnosis and Treatment of Acute Medical Disorder*  
         [Murphy] 543  
     *Endocrinology of Woman* [Hamblen] 615  
     *Falling Sickness* [Temkin] 654  
     Feldman M 653  
     Golden, R 877  
     Hamblen, E C 615  
     Haymaker, W 653  
     Hilleboe, H E 772  
     *History of Surgical Anesthesia* [Keys] 877  
     Janney, J C 772  
     Kagan, S R 654  
     Keys, T E 877  
     Lyle, D J 653  
     *Mass Radiography of Chest* [Hilleboe & Morgan] 772  
     *Medical Care and Health Services for Rural People* 543  
     *Medical Gynecology* [Janney] 772  
     *Medical Uses of Soap* 544  
     *Microbial Antagonisms and Antibiotic Substances* [Waks-  
         man] 654  
     *Modern Medical World* [Kagan] 654  
     Morgan, R H 772  
     Moseley, H F 616  
     Murphy, F D 543  
     *Neuro-ophthalmology* [Lyle] 653  
     1944 Year Book of Industrial and Orthopedic Surgery 615  
     *Peripheral Nerve Injuries* [Haymaker & Woodhall] 653  
     *Radiologic Examination of Small Intestine* [Golden] 877  
     *Shoulder Lesions* [Moseley] 616  
     Stern, R A 772  
     Temkin, O 654  
     *Trauma in Internal Diseases* [Stern] 772  
     Waksman, S A 654  
     Woodhall, B 653  
 BOOKS - War victims 711 - misc  
 BOSTON GASTROENTEROLOGICAL SOCIETY, Apr 24 544 - n  
 BOSTON MEDICAL HISTORY CLUB, Feb 11 206 - n  
 BOSTON SOCIETY OF BIOLOGISTS, Feb 20 240 - n  
 BOSTON SURGICAL SOCIETY (See Notes) 682 - misc  
 BOSTON UNIVERSITY Course for Discharged Medical Officers,  
     Mar 15-Sept 15 240 - n  
     new surgical head 36 - misc  
     psychiatry program 543 - misc  
     School of Medicine Alumni Association, May 10-11 616 - n  
 BRAIN cyst [Heusner & others] 511 - cr  
     tumors [Sweet] 234 - cr  
 BREAD 874 - c  
 BRONCHI Tumors [King & others] 843 - cr  
 BRONCHIECTASIS [Bobrowitz & others] 141\*

## C

CANCER 311 - c  
     clinics Cured 545 - mdph  
     research Grants and fellowships 712 - n  
 CANON, WALTER B 98 - o  
     memorial 846 - c, 848 - misc  
 CARCINOMA [Bartlett & others] 161 - cr  
     [Chapman & others] 739 - cr  
     [Clifford & others] 564 - cr  
     [Moore & others] 28 - cr  
     [Parsons & Meigs] 860 - mp  
     [Soutter & others] 703 - cr  
     [Sowles & others] 766 - cr  
     [Volwiler & others] 537 - cr  
 CARDIOVASCULAR disease [Traum & Wilcox] 82\*  
 CARIES, dental [Getting] 757, 791 - mp  
 CAROTENE [Holmes & others] 47\*  
 CARR, EARL BURTON (See Deprivation of licenses) 490 - c  
 CASE histories [Heath] 251\*  
 CERVIX carcinoma [Richardson & others] 675 - cr  
 CESAREAN section [Waters] 849\*  
 CHEMOPROPHYLAXIS 487 - c  
 CHILDREN'S HOSPITAL 769 - c  
     *Christian Science Journal* [Kilpatrick] 136 - c  
 CLAVICLE Fracture Nail fixation [Lee] 222\*  
 COLON carcinoma [Soutter & others] 703 - cr  
     surgery Use of phthalylsulfathiazole [Thomas & Dalan  
         431\*  
 COLOSTOMY [Foisie] 464\*  
 COMMITTEE ON GROWTH 311 - c  
 COMMONWEALTH FUND 424 - c  
 COMMUNICABLE-DISEASE control, symposium on, Jan 22,  
     102 - n  
 CRANIAL defects [Carmody] 395\*

## D

DDT solution [Downing] 101 - c  
 DEATHS  
     Abbott, Clifton S 100  
     Alexandrov, Vitaly J 425  
     Alley, Ernest J 807  
     Atwater, James B 748  
     Ayer, Thomas H 748  
     Burgess, Charles J 425  
     Cannon, Walter B 98 - o  
     Cavanaugh Mortimer T 99  
     Churchill, Frank S 389  
     Cousens, Nicholas W 518  
     Cutler, Charles H 100  
     Davenport, Benita C 68  
     Drummev, Nicholas D 68  
     Elliott, John J 572  
     Ellis, Edward K 847  
     Evans, Miner H A 748  
     Fessenden, Charles H 644  
     Goodwin, James J 99  
     Gunter, Fred C 681  
     Jack, Lewis H 710  
     Kaplan, Boris 99  
     Keith, Theodore K 205  
     Knowlton, Edward A 154  
     Landesman, Henry M 771  
     Lee, Frank R 205  
     Leonard, Edward D 100  
     McLeod, Melvin S 710  
     McNamara, John J 100  
     Metzger, Butler 681  
     Mulligan, Francis J 277  
     Overlander, John E 847  
     Piper, Frank J 572  
     Quest, James F 847  
     Robbins, Fred G 205  
     Rosenau, Milton J 572  
     Sanders, Loren A 876  
     Scenna, Donato T 425  
     Scott, Nathaniel H 277  
     Stevens, Harry L 277  
     Sullivan, Cornelius A 518  
     Taylor, Herbert L 100

Timmins, Edward F 277  
 Treanor, John P 847  
 Woodward, Samuel B 277; 517 - o  
 Young, J Herbert 389  
 DENNY, FRANCIS P retires 69 - misc  
 DEPRIVATION of licenses [Gallupe] 490, 711 - c  
 DERMATITIS [Downing] 101 - c  
 [Ronchese] 665\*  
 DIABETES, etiology Psychogenic factors [Gendel & Benjamin] 556\*  
 mellitus [Greenblatt & Root] 119\*, [Joslin] 442, 476 - mp  
 DIABETIC COMA Diagnosis 310 - c  
 [Haigh] 312 - c  
 therapy [Gorman & others] 500\*  
 DIPHTHERIA epidemic 202 - c  
 DISABILITY waiver 276 - e, 278 - c  
 DRUGS, dangerous 69 - misc  
 habit forming 571 - mms

## E

EASTERN ASSOCIATION OF ELECTROENCEPHALOGRAPHERS,  
 Apr 12, 712 - mr  
 ECONOMICS, medical [Sinai] 122\*  
 EDITORIALS  
 Action and reaction 238  
 Annual meeting (Massachusetts Medical Society) May 21-  
 23, 643  
 Break for margarine 388  
 Cannon, Walter B, memorial 846  
 Cardiac murmurs 348  
 Care of patient 846  
 Chemistry of penicillin 770  
 Clinical investigation by Veterans Administration 97  
 Committee on growth 311  
 Dangers of chemoprophylaxis 487  
 "Diphtheria rebounds" 202  
 Dosage of penicillin 706  
 Early diagnosis and treatment of diabetic coma 310  
 Effect of vitamin supplements 708  
 "Else whence this pleasing hope" 167  
 Federal support for science in peacetime 131  
 Gamma globulin in acute hepatitis 745  
 H R 5296 614  
 Inadequacies of medical care  
 I General considerations 515  
 II Those concerning its distribution and cost 539  
 III Those concerning its quality 569  
 IV Those concerning its adjuncts 613  
 V How they can be corrected 644  
 Licensing of osteopathic physicians in Massachusetts 239  
 Medical center for children at Children's Hospital 769  
 Medical sociology 32  
 Merger and medical service 453  
 Motorcade 747  
 National Hospital Day 680  
 National Social Hygiene Day 166  
 New American Medical Association program 424  
 New deal for Veterans Administration 201  
 New York City restricts sale of penicillin 66  
 One hundred and sixty-fifth anniversary 805  
 Pediatric survey 487  
 Penicillin 875  
 and syphilis A second warning 516  
 treatment of empyema 387  
 Pepper bill 32  
 Quarter century of progress 570  
 Ration's end? 276  
 Refresher course for physicians 97 - mms  
 Routine blood test for syphilis 67  
 School health policies 349  
 Sixty years of nursing service 680  
 Staff of life 874  
 Teaching hospitals 540  
 Tetanus prophylaxis and treatment 806  
 "To do something for welfare of mankind" 424  
 (Albrecht) Von Haller—physician extraordinary 454  
 Waiver of disability 276  
 ELECTROENCEPHALOGRAPHY STUDY [Greenblatt & others] 119\*  
 EMBOLISM pulmonary [McGinn] 610 - cr  
 EMPYEMA [Strieder & Lynch] 1\*  
 therapy Penicillin 387 - c

ENDOCARDITIS bacterial [Kranes] 634 - cr  
 subacute bacterial [Favour & others] 71\*, [Short & others] 90 - cr  
 EPISTAXIS [Amsden] 81\*  
 ESOPHAGUS stricture [Benedict & others] 801 - cr  
 ETHER Inhalers [Ford] 713\*  
 EWING'S SARCOMA [Franseen & others] 304 - cr  
 [Nathanson & others] 127 - cr

## F

FLUORINE [Getting] 757, 791 - mp  
 FROG [Robbins & others] 784\*

## G

GALL BLADDER, hemorrhage [Hudson & Johnson] 438\*  
 tumors [Miller] 473\*  
 GAUCHER'S disease [Fienberg & Quigley] 527\*  
 GERMAN Medicine during war [Zollinger] 322\*  
 GLOBULIN 745 - c  
 GLOMERULONEPHRITIS [Klemperer & others] 379 - cr  
 GLUCOSE tolerance test [Campbell & Tagnon] 216\*  
 GRANULOMA inguinale [Berkowitz] 625\*  
 GREATER BOSTON MEDICAL SOCIETY, Feb 19, 168, Mar 312, Apr 9, 458 - n

## H

HABIT-forming drugs 571 - mms  
 HARVARD MEDICAL ALUMNI ASSOCIATION, July 3, 682, 808  
 HARVARD, refresher courses 100 - misc  
 HARVARD SCHOOL OF PUBLIC HEALTH changes 135 - misc  
 HEALTH insurance plans [Faxon] 86\*  
 legislation [Goldmann] 655, 687, 727, 749\*  
 HEART DISEASE [Boyer] 111\*, [Lium] 691\*  
 diet [Bridges & others] 573\*  
 HEART MURMURS 348 - c  
 [Merrill] 355 - c  
 HEART SURGERY [Strieder] 504, 531 - mp  
 HEMANGIOMA [Sweet] 234 - cr  
 HEMATOLOGY [Dameshek] 829 - mp  
 HEMATOMA [Rose] 582\*  
 HEMOCHROMATOSIS [Bauer & others] 866 - cr  
 HEPATITIS, acute 745 - c  
 HEPATOMA [Townsend & others] 673 - cr  
 HODGKIN'S disease VI Clinical diagnosis [Jackson & Park] 37\*  
 VII Treatment and prognosis [Jackson & Parker] 103\*  
 HOSPITALS  
 New England Hospital for Women and Children, Feb 136, Mar 7, 312, Apr 4, 426, May 2, 572, June 6, 71 July 9, 878 - n  
 (Joseph H) Pratt Diagnostic Hospital medical conference program, Feb 1-27, 136, Mar 1-29, 312, Apr 3-26, 45 May 3-31, 616 - n  
 HOSPITALS Teaching 540 - c  
 H R 5296 614 - c  
 HYDRONEPHROSIS [Colby] 451 - cr

## I

ICE CREAM and vitamins [Holmes & others] 47\*  
 INDUSTRIAL HEALTH CONGRESS, Sept 30-Oct 3, 878 - n  
 INFECTIONS, local [Rose & Hurwitz] 291\*  
 INHALERS [Ford] 713\*  
 INSULIN syringes, dangers [Collins & others] 367\*  
 INTESTINE, acute obstruction [Moses] 78\*  
 INTESTINES obstruction [Foisie] 498\*  
 INTRATHORACIC lesions [Overholt & Wilson] 169\*  
 INTUSSUSCEPTION [Atwood] 329\*

## J

JAUNDICE Serum [Grossman & Saward] 181\*  
 JEJUNUM carcinoma [Sowles & others] 766 - cr

K

KIDNEY disease [Jacobson & others] 798 - cr  
[Linenthal] 307 - cr  
necrosis [Hertig] 416 - cr

L

LABORATORIES, medical 876 - mdph  
LABORATORY values, normal 24 - cr  
LAHEY (Frank H.) (See Notes) 682 - misc  
LEUKEMIA 167 - e  
monocytic [McCarthy & Karcher] 787\*  
in radiologists [Ulrich] 45\*  
LIVER abscess, pyogenic [Flynn] 403\*  
cirrhosis [Short & others] 90, 566 - cr  
degeneration [Homburger] 683\*  
disease [Campbell & Tagnon] 216\*  
LUNG carcinoma [Baker] 383 - cr  
metastasis [Schatzki & others] 839 - cr  
LUNGS, actinomycosis [Miller & others] 508 - cr  
LYMPHOMA [Ellis] 163 - cr  
malignant [Davenport & others] 62, [Taylor & others]  
701 - cr

M

MACDONALD, EDMOND J. (See Deprivation of licenses) 490 - c  
MACY FOUNDATION 205 - misc  
MALARIA Relapsing vivax [Gordon & others] 519\*  
MALPRACTICE liability 134, 542  
MARCHAND, JEAN C. (See Deprivation of licenses) 711 - c  
MARGARINE 388 - e  
MASSACHUSETTS CENTRAL HEALTH COUNCIL, Apr 9, 652 - mr  
MASSACHUSETTS DEPARTMENT OF MENTAL HEALTH [Perkins]  
101 - c  
MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH  
Blood and blood derivatives program 389  
Cancer clinics Cured 543  
Crippled children clinics, Jan 18-29, 100, Feb 1-26, 135,  
Mar 1-26, 311, Apr 1-26, 456, May 1-28, 615, June  
3-25, 748, July 1-23 876  
Diseases, communicable, for Nov 1945, 69, Dec, 135, Jan,  
1946, 390, Feb, 456, Mar, 681, Apr, 771  
Distribution of penicillin stopped 100  
Laboratories, medical 876  
Notes 572, 710  
Psittacosis 808  
Serum globulin 615  
MASSACHUSETTS First bacteriologic laboratory [Wails]  
391 - c  
MASSACHUSETTS HOSPITAL ASSOCIATION, Mar 11, 240 - n  
MASSACHUSETTS MEDICAL SOCIETY  
Annual meeting 643 - e  
Annual oration Gastric surgery [Lahey] 809  
Applicants for fellowship 351  
Blue Triangle 68  
Council, annual meeting, May 21, 542  
executive committee, Jan 9, 205, Apr 24, 709  
special meeting, Jan 9, 338, Apr 10, 455  
proceedings, Feb 6 591  
Gastric surgery [Lahey] 809  
Habit-forming drugs Marking of prescriptions 571  
Nutrition and war [Youmans] 773  
One hundred and sixty-fifth anniversary 805 - e  
Postgraduate medical education 97 - e  
Postwar planning 34  
Program of one hundred and sixty-fifth anniversary, May  
21-23 648  
Resolution concerning review lecture course 748  
Review lecture course Feb 18-Mar 13, 203, program  
Mar 18-Apr 15, 349, changes 456, program Apr 17-  
May 15, 489, resolution adopted 748  
Shattuck Lecture Nutrition and war [Youmans] 773  
Surplus government property 455  
Telephone listing 542  
Treasurer's report covering refund distribution 542  
MASSACHUSETTS MEDICO-LEGAL SOCIETY, May 22, 682 - n  
MASSACHUSETTS PHYSIOTHERAPY ASSOCIATION 544 - n  
MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS, May 8,  
544 - n

McGILL -- anesthesia, 277 - misc  
McLEAN HOSPITAL 711 - misc  
MECKEL'S diverticulum [Atwood] 329\*  
MEDICAL care 846 - e  
Butler 260\*  
Distribution [Bauer] 225\*, [Clark] 53\*  
[Lane] 808 - c  
Foreign programs [Goldmann] 155\*  
Inadequacies [Nye]  
I General Considerations 515 - e  
II Those Concerning Its Distribution and Cost 539 - e  
III Those Concerning Its Quality 569 - e  
IV Those Concerning Its Adjuncts 613 - e  
V How They Can Be Corrected 644 - e  
National problem [Rogers] 296\*  
MEDICAL LIBRARY ASSOCIATION Mar 25-27, 356 - n,  
711 - mr  
MEDICINE Practice [Miller] 823\*  
MEDICOLEGAL ABSTRACTS Malpractice liability 542  
Practice Government regulation 355, 425, 645  
Relation of patient and physician liability for mal  
practice 134  
MEETING Annual (Massachusetts Medical Society) 643-e  
MENINGITIS Meningococcal Recurrent [Weinstein & Stan  
ley] 364\*  
Penicillin therapy [Kinsman & D'Alonzo] 459\*  
MENTAL breaking points [Dynes] 42\*  
MERTHIOLATE, tincture sensitivity [Lipson] 441\*  
METABOLISM carbohy drate [Hurwitz & Jensen] 327\*  
METHIONINE [Homburger] 683\*  
MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY, Mar 20,  
392 - n  
MILITARY medicine [Wetherbee] 652 - c  
merger Medical aspects 453 - e  
MISSTATEMENT [Bailey] 615 - c  
MONONUCLEOSIS infectious [Slade] 753\*  
MOTORCADE 747 - e  
MYELOMA [Ropes & others] 763 - cr  
MYOCARDITIS [Sprague] 420 - cr

N

NATIONAL HOSPITAL DAY 680 - e  
NATIONAL SOCIAL HYGIENE DAY 166 - e  
NECK aneurysm [Boyd] 370\*  
NEPHROLITHIASIS [Aub & others] 59 - cr  
NEPHROSIS [Ropes & others] 763 - cr  
NEURINOMA [Garrey & others] 535 - cr  
[McKittrick & others] 194 - cr  
NEW ENGLAND DERMATOLOGICAL SOCIETY, Apr 10, 458 - n  
NEW ENGLAND HEART ASSOCIATION  
Low-sodium diet and free fluid intake in treatment of con  
gestive heart failure [Bridges & others] 573\*  
Meetings, Feb 26, 206, June 3, 712 - n  
NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN, Feb 7,  
136, Mar 7, 312, Apr 4, 426, May 2, 572, June 6  
712, July 9, 878 - n  
New England Journal of Medicine History 570 - e  
self-supporting [Garland] 572 - c  
NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY,  
May 29, 616 - n  
NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY, May 8,  
544 - n  
NEW ENGLAND PATHOLOGICAL SOCIETY, Feb 21, 240 - n  
NEW ENGLAND PEDIATRIC SOCIETY, Feb 28, 206, May 15,  
616 - n  
NEW ENGLAND ROENTGEN RAY SOCIETY, May 17, 572 - n,  
771 - mr  
NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE, Jan 16, 70,  
Feb 20, 206, May 16, 654 - n  
NEW ENGLAND SURGICAL SOCIETY  
Motivations and opportunities [Miller] 823  
NEW HAMPSHIRE MEDICAL SOCIETY  
Epistaxis [Amsden] 81\*  
Deaths  
Abbott, Clifton S 100  
Cutler, Charles H 100  
Sanders, Loren A 876  
Scott, Nathaniel H 277  
Taylor, Herbert L 100  
NEW YORK ACADEMY OF MEDICINE, Oct. 7-18, 544 - n

NONSERVICE-connected illness 543 - misc  
NORTON medical award 392 - n  
NURSING 680 - e  
NUTRITION [Youmans] 773 - mms

## O

(DR.) O'HARA appointed dean at Tufts 645 - misc  
OPHTHALMOLOGICAL STUDY COUNCIL, April 1-June 1, 240 - n  
OSLER, SIR WILLIAM [Fitz] 617\*  
OSTEOPATHIC physicians Licensing 239 - e

## P

PANCREAS Carcinoma [Moore & others] 28 - cr  
PARALYZED persons Rehabilitation [Munro] 207\*  
PARATHYROID adenoma [Butler] 125 - cr  
PASSANO FOUNDATION award 645 - misc  
PEDIATRIC survey 487 - e  
PEDICULOSIS capitis [Ronchese] 665\*  
PENICILLIN 66 - e, 100 - mdp, 387, 516, 706, 770, 875 - e  
    [Bobrowitz & others] 141\*  
    [Hirsh & others] 853\*  
    [Kinsman & D'Alonzo] 459\*  
    [Rose & Hurwitz] 291\*  
    [Telfer] 748 - c  
PENTOTHAL sodium anesthesia [Shannon & Gardner] 15\*  
PEPPER BILL 32 - e  
PEPTIC ULCER [Ulfelder & others] 485 - cr  
    among soldiers [Halsted & Weinberg] 313\*  
    therapy [Moore & others] 241\*  
PERICARDITIS [Bland] 608 - cr  
    [King] 341 - cr  
PHI DELTA EPSILON SOCIETY, Jan 17, 70 - n  
PHLEBOTROMBOSIS [Moses] 288\*  
PHYSICAL medicine [Watkins] 584, 628 - mp  
PLASMA Commercial [Grossman & Saward] 181\*  
    surplus 389 - mdp  
PLEURISY alternating [Bird] 491\*  
    (ELLA SACHS) Plotz Foundation 206 - n  
PNEUMOTHORAX spontaneous [Greene] 639 - cr  
POISONING Industrial 69 - misc  
POSTGRADUATE MEDICAL EDUCATION 97 - e  
    Feb 18-Mar 13, 203, program Mar 18-Apr 15, 349,  
    changes 456, program Apr 17-May 15, 489, reso-  
    lution adopted 748 - mms  
POSTWAR planning 34, 542 - mms  
    reaction 238 - e  
PRACTICE Government regulation 355, 425  
    Medical [McKittrick] 188\*  
    Regulations 645  
PRACTITIONER, general [Atkinson] 456 - c  
(JOSEPH H.) PRATT DIAGNOSTIC HOSPITAL, medical confer-  
ence program, Feb 1-27, 136, Mar 1-29, 312, Apr 3-26,  
458, May 3-31, 616 - n  
PREGNANCY complications [Rose] 582\*  
    [Robbins & others] 784\*  
    normal [Hurwitz & Jensen] 327\*  
PRIZE contest 168 - n  
PROGRESS, MEDICAL  
    Abdominal surgery [Allen] 408  
    Diabetes mellitus [Joslin] 442, 476  
    Fluorine and dental caries [Getting] 757, 791  
    Gynecology Carc noma of vulva [Parsons & Meigs] 860  
    Hematology [Dameshek] 829  
    Normal growth and development during adolescence  
    [Stuart] 666, 693, 732  
    Research in physical medicine [Watkins] 584, 628  
    Surgery of heart and structures related to it [Strieder]  
    504, 531  
    Syphilis [Crawford] 332, 372  
    Urology [Colby] 560  
PSITTACOSIS 808 - mdp  
PSYCHIATRY program at Boston University 543 - misc  
PSYCHOSOMATIC backache [Sargent] 427\*  
PUBIS Ewing's sarcoma [Nathanson & others] 127 - cr  
PUBLIC HEALTH 424 - e

## R

RATIONING 276 - e  
RECTOSIGMOID carcinoma [Simeone] 344 - cr  
RHEUMATIC fever [Rosenberg] 148\*  
    fellowships 878 - n  
RIB tumors [Franseen & others] 304 - cr  
RIBOFLAVIN [Holmes & others] 47\*  
ROENTGEN rays History [Woodbury] 682 - c  
RONKA (ENSIO K F) 682 - misc

## S

SARCOMA [Nathanson & others] 127 - cr  
SCARLET FEVER [Withington] 711 - c  
SCHOOL health 349 - e  
SCIENCE Federal support 131 - e  
SCLEROSIS coronary [Williams] 231 - cr  
SERUM globulin 615 - mdp  
SHOCK, medical [Davidson & others] 279\*  
    therapy Electric [Norman & Shea] 857\*  
SKIN sensitivity [Lipson] 441\*  
SMITHWICK, REGINALD H 36 - misc  
SOCIETIES  
    American Association for Study of Goiter, June 20-22,  
    312 - n  
    American College of Chest Physicians, June 29, 544 - n  
    Boston Gastroenterological Society, Apr 24, 544 - n  
    Boston Medical History Club, Feb 11, 206 - n  
    Boston Society of Biologists, Feb 20, 240 - n  
    Greater Boston Medical Society, Feb 19, 168, Mar 12,  
    312, Apr 9, 458 - n  
    Harvard Medical Alumni Association, July 3 808 - n  
    Massachusetts Hospital Association, Mar 11, 240 - n  
    Massachusetts Medico-Legal Society, May 22, 682 - n  
    Massachusetts Society of Examining Physicians, May 8,  
    544 - n  
    Medical Library Association, Mar 25, 26, 27, 356 - n  
    Middlesex South District Medical Society, Mar 20, 392 - n  
    New England Dermatological Society, Apr 10, 458 - n  
    New England Heart Association, Feb 26, 206, June 3,  
    712 - n  
    New England Obstetrical and Gynecological Society, May  
    29, 616 - n  
    New England Oto-Laryngological Society, May 8, 544 - n  
    New England Pathological Society, Feb 21, 240 - n  
    New England Pediatric Society, Feb 28, 206, May 15,  
    616 - n  
    New England Roentgen Ray Society, May 17, 572 - n,  
    771 - mr  
    New England Society of Physical Medicine, Jan 16, 70,  
    Feb 20, 206, May 16, 654 - n  
    Phi Delta Epsilon Society, Jan 17, 70 - n  
    South End Medical Club, Jan 15, 36, Feb 19, 240,  
    Mar 19, 392, June 18, 808 - n  
    Suffolk District Medical Society, Apr 27, 518 - n  
    Tufts Medical Alumni Association, Apr 10, 426 - n  
SOCIOLOGY, MEDICAL  
    32 - e  
    Foreign programs of medical care and their lessons [Gold-  
    mann] 155  
    Health bills pending in congress [Goldmann] 655, 687,  
    727-749  
    Health-insurance plans [Faxon] 86  
    Medical economics [Sinai] 122  
    Medical practice and its future [McKittrick] 188  
    Minority views on improving medical care [Butler] 260  
    Point of view of organized medicine toward distribution  
    of medical care [Bauer] 225  
    Practical considerations in planning and conduct of national  
    medical-care program [Rogers] 296  
    Problems in distribution of medical care [Clark] 53  
    Some clinical aspects of social medicine [Cannon] 20  
SODIUM diet [Bridges & others] 573\*  
SOUTH END MEDICAL CLUB, Jan 15, 36, Feb 19, 240, Mar  
19, 392, June 18 808 - n  
SPINE Tuberculosis [Aufranc & others] 94 - cr  
SPLEEN Rupture [Waugh] 621\*  
SPOROTRICHOSIS [Flo & Smith] 50\*  
STOMACH [Volwiler & others] 537 - cr  
    carcinoma [Chapman & others] 739 - cr

STOMACH surgery [Lahey] 809 - mms  
 ulcer [Halsted & others] 741 - cr  
 STOMACH TUMORS [Clifford & others] 564 - cr  
     [Ellis] 163 - cr  
     [Garrey & others] 535 - cr  
     [McKittrick & others] 194 - cr  
 STREPTOCOCCAL infection [Withington] 711 - c  
 SUFFOLK DISTRICT MEDICAL SOCIETY, Apr 27, 518 - n  
 SULFONAMIDES Pathologic effects [Jacobson & others]  
     798 - cr

SURGICAL wound infection [Weinstein] 184\*  
 SURPLUS government property 455 - mms  
 SYPHILIS [Crawford] 332, 372 - mp  
     blood tests 67 - c  
     osseous [Exley & Newton] 661\*  
     and penicillin 516 - c

## T

TELEPHONE listing 542 - mms  
 TETANUS Prophylaxis 806 - c  
 TRANSPLANTATION [Waugh] 621\*  
 TRENCH foot disability [Paddock] 433\*  
 TUBERCULOSIS Pulmonary [Bird] 491\*, diagnosis [Bobrowitz & Dwork] 10\*  
 TUFTS ALPHA OMEGA ALPHA, Feb 27, 168 - n  
 TUFTS MEDICAL ALUMNI ASSOCIATION, Apr 10, 426 - n  
 TULAREMIA [Warring & Ruffin] 137\*  
 TUMORS [Clifford & others] 564 - cr  
     diagnosis 876 - misc  
     [Garrey & others] 535 - cr  
     [Volwiler & others] 537 - cr  
 TYPHOID-bacillus infection [Weinstein] 184\*

## U

UNITED STATES PUBLIC HEALTH SERVICE 392 - n  
 URINARY incontinence [Muellner] 400\*  
     tract trauma [Weens & others] 357\*  
 URINATION control in paralyzed persons [Munro] 207\*  
 UROLOGY award 136 - n  
     [Colby] 451, 560 - mp

## V

VAGUS nerves Resection [Moore & others] 241\*  
 VETERANS Cardiovascular disease [Traum & Wilcox] 82\*  
     Administration 201 - c, clinical investigation 97 - c  
     VITAMIN supplements 708 - c  
     (VLBRECHT) Von HALLER 454 - c  
 VULVA Carcinoma [Parsons & Meigs] 860 - mp

## W

WOLFF-PARKINSON-WHITE syndrome [Boyer] 111\*  
 (SAMUEL B.) WOODWARD 517 - o  
 WOUNDS Secondary closure [Foisie] 320\*

## X

X-RAYS History [Means] 848 - c

## Y

YUGOSLAV relief [Schick & others] 876 - c



# AUTHOR INDEX

## A

ADAMS, M A 279\*  
ALEXANDER, E Jr 258\*  
ALLEN, A W 408 - mp, 741, 870 - cr  
AMSDEN, H H 81\*  
ANGELUSCHEFF, Z 876 - c  
ATKINSON, F C 456 - c  
ATWOOD, W G 329\*  
AUB, J 59 - cr  
AUFRANC, O E 94 - cr

## B

BAILEY, F J 615, 682 - c  
BAKER, M P 383 - cr  
BARTLETT, M K 161 - cr  
BASSIN, S 141\*  
BAUER, L H 225\*  
BAUER, W 866 - cr  
BENEDICT, E B 739, 801 - cr  
BENJAMIN, J E 556\*  
BERG, R T 449 - cr  
BERKOWITZ, J 625\*  
BIRD, K T 491\*  
BLAND, E F 196, 608 - cr  
BOAS, L C 367\*  
BOBROWITZ, I D 10, 141\*  
BOYD, P L 370\*  
BOYER, N H 111\*  
BRAILEY, A G 449 - cr  
BRIDGES, W C 573\*  
BROWN, E A 468\*  
BUTLER, A M 125 - cr, 260\*, 798 - cr

## C

CAMPBELL, J A 216\*  
CANAVAN, F T 47\*  
CANWON, I M 20\*  
CARMODY, J T B 393\*  
CHAPMAN, E M. 739 - cr  
CHAPMAN, W P 241\*  
CLARK, D A 53\*  
CLIFFORD, M H 564 - cr  
COLBY, F H 451 - cr, 560 - mp,  
798 - cr  
COLLENS, W S 367\*  
COPE, O 59 - cr  
COTZIAS, G C 270 - cr  
CRAWFORD, G M 332, 372 - mp  
CRAWFORD, J D 379 - cr

## D

DALAND, E M 127 - cr, 431\*  
D'ALONZO, C A 459\*  
DAMESHEK, W 829 - mp  
DAVENPORT, L 62 - cr  
DAVIDSON, C S 279\*  
DIMMLER, C L, Jr 545\*  
DONALDSON, G A 194 - cr  
DOWLING, H F 853\*  
DOWNING, J G 101 - c  
DOYLE, W C 784\*  
DUNPHY, J E 545\*  
DWORK, R E 10\*  
DYNES, J B 42\*

## E

EDLIN, J S 441\*  
ELLERBROOK, L D 519\*  
ELLIS, D S 163 - cr  
EMERSON, K 876 - c  
ESLICK, R L 258\*  
EXLEY, M. 661\*

## F

FAVOUR, C B 71\*  
FAXON, N W 86\*  
FEFFER, H L 853\*  
FIENBERG, R 527\*  
FITZ, R 617\*  
FLO, S C 50\*  
FLORENCE, T J 357\*  
FLYNN, J E 403\*  
FOISIE, P S 320, 498\*  
FORD, W W 713\*  
FRANSEEN, C C 304 - cr  
FRIEDENBERG, R 552\*

## G

GALLUPE, H Q 490, 711 - c  
GARDNER, W J 15\*  
GARLAND, J 572 - c  
GARREY, W 535 - cr  
GENDEL, B R 556\*  
GETTING, V A 757, 791 - mp  
GIBSON, J G II 71\*  
GINSBERG, H S 826\*  
GOLDMANN, I 155, 655, 687, 727, 749\*  
GORDON, H H 519\*  
GORMAN, R V 500\*  
GRAY, W 578\*  
GREENBLATT, M 119\*  
GREENE, J E 639 - cr  
GROSSMAN, C M 181\*

## H

HAIGH, G W 312 - c  
HALE, C H 28, 94, 196 - cr  
HALSTED, J A 313\*, 741 - cr  
HARWOOD, R 500\*  
HEATH, C W 251\*  
HERRERA, R E 485, 701, 801 - cr  
HERTIG, A T 416 - cr  
HESSELBROCK, W B 519\*  
HEUSNER, A P 511 - cr  
HILLIARD, C M 391 - c  
HIRSH, H L 853\*  
HOERR, S O 545\*  
HOLMES, A D 47\*  
HOLMES, G W 379 - cr  
HOMBURGER, F 683\*  
HUDSON, P B 438\*  
HURWITZ, D 291, 327\*

## J

JACKSON, H Jr 37, 103\*  
JACOBSON, B 798 - cr  
JANEWAY, C A 71\*  
JENSEN, D 327\*  
JOHNSON, P P 438\*  
JONES, C P 47, 241\*, 763 - cr  
JOSLIN, E P 442, 476 - mp

## K

KARCHER, P H 787\*  
KILPATRICK, W D 136 - c  
KING, D S 341, 843 - cr  
KINSMAN, J M 459\*  
KLEMPERER, F W 379 - cr  
KRABEK, W 468\*  
KRANES, A 634 - cr  
KUZMESKI, J W 47\*

## L

LAHEY, F H 809 - mms  
LANE, J D 808 - c  
LEE, H G 222\*  
LEVINE, S A 71\*  
LEWIS, J H 279\*  
LINENTHAL, A J 307 - cr  
LINGLEY, J R 511, 508, 537, 673,  
675, 793, 801, 870 - cr  
LIPPINCOTT, S W 519\*  
LIPSON, L 441\*  
LIUM, R 691\*  
LONNERGAN, L R 114\*  
LYNCH, J P 1\*

## M

MARBLE, A 519\*  
MC CARTHY, F P 787\*  
MCCLINTOCK, J K 114\*  
MCGINN, S 610 - cr  
MCKITTRICK, L S 188\*, 194 - cr  
MC MANUS, J F 17\*  
MEANS, P C 848 - c  
MEIGS, J V 843 - cr, 860 - mp  
MERRILL, D 355 - c  
MILLER, C C. 508 - cr  
MILLER, D 473\*  
MILLER, J R 823\*  
MOLONEY, W C 114\*  
MOORE, F D 28 - cr, 241\*  
MORITZ, A R 270 - cr  
MORRIS, D P 258\*  
MOSES, W R 78, 288\*  
MUELLNER, S R 400\*  
MUNRO, D 207\*  
MURRAY, J 119\*

## N

NATHANSON, I T 127 - cr  
NEWMAN, J H 357\*  
NEWTON, A W 661\*  
NORMAN, J 857\*

## O

OVERHOLT, R H 169\*

## P

PADDOCK, F K 433\*  
PALMER, R S 272 - cr  
PARKER, F Jr 37, 103, 784\*  
PARSONS, L 860 - mp  
PENNER, S L 523\*  
PERRINS, C T 101 - c  
PETERS, M 523\*

## Q

QUIGLEY, G E 527\*

## R

RICHARDSON, W 62, 90, 482, 675 - cr  
RISEMAN, J E F 578\*  
ROBBINS, S L 784\*  
ROGERS, E S 296\*  
RONCHESE, F 665\*  
ROOT, H F 119\*  
ROPES, M W 763 - cr

# INDEX TO VOLUME 234

OSE, D 291 582\*  
 OSENBURG, D H 148\*  
 UFFIN, J S JR 137\*

## S

ARGENT, M 427\*  
 AWARD, E W 181\*  
 BARTZKI R 701, 703, 766, 839 - cr  
 BICK, B 876 - c  
 BULZ, M D 127, 161 - cr, 241\*  
 CANNON, E W 15\*  
 CHA, J T 857\*  
 CORT, C L 90, 566 - cr  
 CROWE, F A 344, 766 - cr  
 DAL, N 122\*  
 DUFFINGTO, R 468\*  
 EADE, JOHN DER 753\*  
 EATH, P E. 50\*  
 EIFFEN, R C 28 - cr  
 EKOL, A J 552\*  
 EUTTER, L 564, 703 - cr  
 EWLES, H K 766 - cr  
 FAGUE, H B 420 - cr  
 FANLEY, E D 364\*  
 FARNES, S 578\*  
 FEVENS, N C. 100 - c  
 FRIEDER, J W 1\*, 504, 531 - mp

STUART, H C 666, 693, 732 - mp  
 SWEET, R H 304, 839 - cr  
 SWEET, W H 234, 511 - cr

## T

TAGNON, H J 216, 279\*  
 TAYLOR, F H L 279\*  
 TAYLOR, G W 701 - cr  
 TELFER, J G 748 - c  
 THOMAS E D 876 - c  
 THOMSON R 431\*  
 TOWNSEND, J H 673 - cr  
 TRAUM A H 82\*  
 TWE, M 152\*

## U

ULFELDER, H 485 - cr  
 ULRICH, H 45\*

## V

VOLWILER, W 537 - cr

## W

WALLS J O 391 - c  
 WARRING, W B 137\*  
 WATERS, E G 849\*  
 WATKINS A L 584, 628 - mp  
 WALGH, R L 621\*  
 WEENS, H S 357\*  
 WEINBERG, H 313\*  
 WEINSTEIN, L 184 364\*  
 WETHERBEE W JR 652 - c  
 WHEELER, E O 573\*  
 WHITE, P D 196 - cr, 500, 573\*  
 WHITE, R R 545\*  
 WILCOX, B B 82\*  
 WILLIAMS, C 231 - cr  
 WILSON N J 169\*  
 WITHINGTON, P R 711 - c  
 WOODBURY F T 682 - c  
 WOOLLEY J S 141\*

## Y

YOUNG, J B 773 - mms

## Z

ZILINSKY, J D 367\*  
 ZOLLINGER, R M 322\*



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## PUTRID EMPYEMA

JOHN W. STRIEDER, M.D.,\* AND JOSEPH P. LYNCH, M.D.†

BOSTON

**PUTRID** empyema has been recognized as a clinical entity for many years and has recently been the subject of a number of excellent reports.<sup>1-4</sup> Nevertheless, many surgeons fail to distinguish it from ordinary pyogenic empyema and, persisting in this misapprehension, treat it as they ordinarily treat this relatively benign lesion, with disastrous results. It is our belief that with a better understanding of the nature of the disease recognition will be prompter, treatment will be more adequate, and the mortality, which has been high, will be lowered.

The report that follows is based on an analysis of patients on the various services at the Boston City Hospital from June, 1934, to January, 1941, and of those on the Thoracic Surgery Service from January, 1938, to January, 1941—90 cases in all. A review of the etiology, bacteriology, pathology and treatment demonstrates that this disease differs strikingly from postpneumonic pneumococcal empyema and other pyogenic empyemas, with which it is so often confused. Furthermore, from the same review it is believed that the advantages of early and radical surgery can be demonstrated.

### DEFINITION

Putrid empyema may be briefly described as a sloughing, gangrenous pleuritis caused by certain anaerobic bacteria acting in symbiosis. Its distinctive characteristic is the presence of extremely foul purulent fluid in the pleural cavity, which gives rise to its name. In almost 100 per cent of these patients the fluid obtained by thoracentesis was described by the operator as foul, stinking, sulfurous or putrid. On the other hand, the pleural fluid from no other patient with empyema was so described, in spite of the fact that a number of cases were due to the colon bacillus. The odor is indeed truly distinctive.

It might be more accurate to call the disease "anaerobic empyema," as has been suggested by

Maier and Grace<sup>1</sup> because, from our own studies and those of others, it appears that putrid empyema is always caused by anaerobic organisms. Melenev<sup>5</sup> states that anaerobic infections are usually foul-smelling. When this is the case, one can be almost certain that he is dealing with anaerobic infection and not, as is so often erroneously inferred, with infection by the colon bacillus, which produces little if any odor. One can be certain that if the odor is foul the anaerobic infection is active, but if it is not, the presence of anaerobes cannot be ruled out. Since, however, there is still disagreement about the bacteriology and since the descriptive name is so distinctive, it seems better to continue the name "putrid empyema" until complete proof of the nature of the infection is at hand.

### INCIDENCE

The number of cases of putrid empyema in any series of patients suffering from empyema varies with certain factors. Our figure is considerably higher than that found in other series, but this is thought to be a corollary of the high percentage of putrid pulmonary infections, such as lung abscess, bronchiectasis, fusospirochetal pneumonitis and pulmonary gangrene, encountered in a large municipal hospital where the economic and hygienic status of the patients is poor. Neuhof and Hirshfeld<sup>6</sup> found the disease in 17 (9 per cent) of 184 children with empyema. In the present series, covering seven and a half years, 530 patients with acute empyema were treated at the Boston City Hospital, and of these, 90 (17 per cent) had putrid empyema. In general, it appears that 5 to 10 per cent of all cases of empyema are found to be putrid.<sup>7</sup>

That the disease is serious can be appreciated from mortality figures. Neuhof and Hirshfeld<sup>6</sup> have reported a mortality of 47 per cent, and Flack<sup>3</sup> one of 66 per cent. In the series of 57 patients reported herein, which were treated in this hospital but not on the Thoracic Surgery Service, most of them before 1938, the mortality was 54 per cent. These patients were treated on general surgical services by methods that would usually have been adequate for postpneumonic empyema but which

\*Assistant professor of thoracic surgery, Boston University School of Medicine, visiting surgeon in charge of thoracic surgery, Massachusetts Memorial Hospitals and Boston City Hospital.

†Assistant to visiting surgeons (thoracic surgery), Boston City Hospital; assistant in surgery (thoracic surgery), St. Elizabeth's Hospital.

according to our criteria, were inadequate for putrid empyema

### ETIOLOGY

Generally putrid empyema is secondary to some type of anaerobic infection of the lung. Most frequently it complicates a lung abscess or a gangrenous

TABLE 1 *Relation of Primary Disease to Mortality*

PRIMARY DISEASE	No of Recoveries Cases		DEATHS	MORTALITY %
Lung abscess	35	18	17	49
Bronchiectasis	12	11	1	8
Tuberculosis	6	2	4	67
Pneumonitis (gangrenous)	24	13	10	43 (23 cases*)
Others (including carcinoma of the lung, 1 trauma, 2 and unknown, 10)	13	6	7	54
Totals	90	50	39	
Average				44

\*One patient left against advice and the outcome is unknown

(fusospirochetal) pneumonitis. In Table 1 are listed the primary diseases in this series, with the mortality rate of the putrid empyema that developed from them.

Graham et al<sup>4</sup> and Rosenblatt<sup>8</sup> state that empyema is one of the most frequent complications of lung abscess. Neuhof and Hirshfeld<sup>2</sup> found that 25 of 104 patients with subacute or chronic lung abscesses developed putrid empyema. Neuhof and his associates<sup>9</sup> also mention this type of empyema as a frequent and serious complication of the surgical drainage of lung abscess. Graham has expressed the belief, with which certain others have agreed, that frequently a lung abscess that has been complicated by putrid empyema heals when the empyema has been adequately drained. Neuhof and his co-workers<sup>9</sup> have denied this, believing that the abscess should be drained at the time of operation for the empyema. In our opinion, spontaneous cures of abscesses depend on the size of the perforation and whether or not drainage resultant on the rupture is adequate. It is our experience that any decision concerning drainage of the abscess at the time of thoracotomy must be taken on the basis of the location of the abscess and the condition of the patient, as will be discussed later.

Graham et al<sup>4</sup> also state that empyema is a not infrequent complication of bronchiectasis. In the postoperative course of lobectomy for bronchiectasis such an empyema has been an all-too-frequent complication. Most of our cases in this group occurred in the course of an acute exacerbation of the bronchiectasis, and might more properly be considered complications of pneumonitis. In 2 of these, a definite cortical abscess could be seen at operation, and undoubtedly rupture of similar abscesses is the mechanism of empyema formation in many of these patients. It is interesting that, as shown in Table 1, when the putrid empyema complicates bronchiectasis the mortality is lower, out of all proportion, than that of the other groups. The significance of

this is conjectural, but may depend on the degree of immunity to the organisms that the patient has built up over a long period through his chronic disease, together with the tendency to localization and stabilization caused by pre-existing pleural adhesions.

### Pneumonitis

Pneumonitis is so designated to distinguish it from pneumococcal pneumonia. These cases are most difficult to understand. Only 3 cases in our personal series fall definitely in this group, but some of them may have been the typical pulmonary gangrene that is included in this category. One of our patients was such a case. Another developed as a complication of fusospirochetal pneumonia, which has been described by Peirce and Field,<sup>10</sup> and others were undoubtedly acute exacerbations of pneumonitis on an underlying bronchiectasis. Careful follow-up studies might have revealed this diagnosis in more cases. Eleven of the 12 patients with bronchiectasis were studied on the Thoracic Surgery Service, which suggests that the diagnosis will be made oftener if its possibility is entertained. In general, the onset of the disease in these patients resembled that of pneumonia, yet its chronicity made this diagnosis untenable. In no case were pneumococci found in the sputum, and roentgenograms of all but 3 demonstrated pleural fluid. The diagnosis in most of these patients was based on the history, for in all but 3, even the physical signs on admission were those of fluid. On the basis of our clinical experience, we believe that the acute stage of all these putrid pulmonary infections is a pneumonitis.

The patients who developed this disease as a complication of tuberculosis probably had secondarily infected blocked cavities that ruptured into the pleura.

The remaining patients include 1 who developed pulmonary gangrene distal to an obstructing carcinoma and 2 who developed it after trauma. In one of the latter it followed the instrumental rupture of a bronchus, the patient having had bronchiectasis secondary to a long-standing obstructing foreign body, for the removal of which bronchoscopy was performed. Thirty-six hours following bronchoscopy he became moribund because of unrecognized tension pneumothorax and anaerobic pleural infection, so that only a closed thoracotomy could be done. He continued to grow worse, and died twenty-four hours later. The other patient, whose case we<sup>11</sup> have previously reported, developed a *Clostridium welchii* infection of the pleura following a stab wound in the chest. This complication, seldom seen in civil life, is frequent in wounds of the chest in wartime.

The unknown group includes 10 patients, 3 of whom died, no autopsies being done. The others received no studies except routine roentgenograms.

Bronchograms would undoubtedly have shown bronchiectasis in some cases. Pilot<sup>12</sup> suggests the mechanism in such cases by assuming the formation of an abscess so close to the pleura that rupture occurs before pulmonary destruction is extensive enough to be apparent clinically.

#### BACTERIOLOGY

The bacteriology of putrid empyema is complicated and uncertain, mainly because of two factors. First, the fact that the infection is due to anaerobic bacteria has prevented complete and accurate correlation of the clinical and bacteriologic studies. Only during the last ten to fifteen years has much study been devoted to these organisms, and even at the present time relatively few hospitals are adequately equipped to do complete anaerobic studies, as pointed out by Meleney.<sup>13</sup> Without such technical facilities the diagnosis cannot be made, for the general experience has been that anaerobic cultures are needed. In our experience, repeated routine cultures of pleural fluid not infrequently show no growth, but the anaerobic culture demonstrates the presence of infection. Second, it seems to be established that the problem of symbiosis is involved in putrid empyema and its related, and usually antecedent, diseases. So general has been the belief that one organism must cause each disease and that Koch's postulates must be satisfied that the work on infections due to the synergistic action of two or more organisms has been retarded. That certain organisms favor the growth and metabolic activity of other species in the same surroundings is well known. It has also been demonstrated that in the development of certain pathologic processes by mixed cultures one species may initiate the inflammatory reaction in the host and the other may complete it. This conception has been suggested by Altemeier,<sup>14</sup> who concludes that although a great deal of work has been done, much remains to be accomplished.

Leeuwenhoek in 1683 first described the fusiform bacillus and the spirochete,<sup>15</sup> and Laennec in 1819 described the first case of pulmonary gangrene. Longacre and Herrmann<sup>16</sup> have discussed the work of Leyden and Jaffe, who in 1867 first associated the spirochete with putrid bronchiectasis and pulmonary abscess, and Kline and Berger<sup>17</sup> mention Plaut (1894) and Vincent (1896) as having identified these organisms and named them as the cause of the mouth infection now known as Vincent's angina.

A review by Fisher and Abernethy<sup>18</sup> states that in 1893 Veillon mentioned the anaerobic streptococcus, which he had isolated from a foul Bartholin's gland. Since that time this organism has most frequently been isolated from foul lesions of the lung and pleura and from puerperal infections. These authors credit Rendu and Rist (1899) with the

description of the association of the anaerobic streptococcus with the gram-negative bacillus.

Until World War I, however, the anaerobes received little attention, but following the armistice much work was done on them. The anaerobic spore-bearing gram-positive bacilli received the greatest attention and consequently are the best understood. Some of these may cause putrid empyema, usually following trauma, but this seldom occurs in civil life.<sup>11, 19</sup> The gram-positive cocci have been recognized, and many attempts to classify them have been made, but much study is still needed. Meleney and his co-workers have been most successful with their researches into microaerophilic streptococci. The gram-negative and gram-positive non-sporulating bacilli have received the least attention of all. In 1905, Weaver and Tunnichiff,<sup>20</sup> after successfully culturing the fusiform bacillus, were unable to produce any pathologic lesions with the pure culture, yet when a mixed culture was used, a gangrenous infection resulted. This inability to produce disease with the pure culture of these organisms gave rise to the impression that they were mere saprophytes, and many still hold this impression.<sup>21</sup> Smith<sup>22</sup> believes that they are not secondary saprophytic invaders. In 150 patients with pulmonary tuberculosis, 6 with asthma and 5 with mycotic lung infections, the fusiform bacilli and the spirochetes were absent in every case, despite repeated examinations. If they were secondary invaders, one would expect them to be present in almost every form of chronic pulmonary disease.

Despite all this work, up to 1928 only about 150 cases of pulmonary fusospirochetal infection had been reported. After this, however, the number of reports relating these organisms to pulmonary gangrene, lung abscess and bronchiectasis greatly increased. Moreover, the excellent work of Smith,<sup>23</sup> Kline<sup>24</sup> and Pilot and Davis<sup>24</sup> has clearly shown that these anaerobes in association — that is, the organisms usually found in Vincent's angina, periodontal infection and pyorrhea alveolaris — are the same as those usually found in putrid lung infections, and that these infections may be produced with them. Smith<sup>25</sup> has reported cases in which contact with a case of Vincent's infection resulted in pulmonary fusospirochetosis and that exactly the same organisms were found in both diseases. More will be said about this in connection with the experimental production of these diseases.

It should be remembered, as has been emphasized by Smith<sup>26</sup> and others, that although these infections are usually referred to as fusospirochetal, this is mainly because these organisms are so easily identified on smear. The anaerobic cocci are always associated with them and are of equal importance.

As revealed in the literature, the bacteriology of putrid empyema seems complex, each author emphasizing a different organism or group of organisms. Fisher and Abernethy<sup>18</sup> stressed the role of the

anaerobic streptococcus, which they were able to find in all the 7 cases they reported. Flack<sup>3</sup> reported 3 cases in which the fusospirochetal organisms seemed to be the important factor. Kline and Berger<sup>27</sup> and Farbman and Danforth<sup>28</sup> have also reported cases in which the fusospirochetal organisms were observed, and the former are especially convinced that these are the pathogenic agent. Maier and Grace<sup>1</sup> describe the cause as a mixed bacterial flora, with the fusiform bacilli, spirochetes and the anaerobic streptococcus those most frequently found. They believe, furthermore, that symbiosis is an important factor in the action of these organisms. Sauerbruch and O'Shaughnessy<sup>29</sup> also name the anaerobes as the cause of putrid empyema.

In Table 2 are presented the results of the bacteriologic findings in this series. The routine pro-

TABLE 2 Bacteriologic Data

ORGANISM	NO OF CASES	RECOVERIES	DEATHS	MORTALITY %
Fusiform bacilli (alone)	18	9	9	50
Streptococcus (strict anaerobe)	8	5	3	38
Streptococcus (facultative anaerobe)	63	35	27	44 (62 cases)
<i>Cl. welchii</i>	1	1	0	0
Totals	90	50	39	

cedure now adopted by the Bacteriology Department is to culture all empyema fluids under anaerobic conditions (cooked-meat medium), as well as aerobically (blood broth and blood-agar plates). Stained smears serve to identify morphologically the fusiform bacilli and spirochetes, and these occasionally grow in the cooked-meat medium. The strictly anaerobic streptococci also grow in the cooked-meat medium and can be subcultured to blood-agar plates that are incubated under anaerobic conditions. The facultative anaerobic streptococci grow both in the cooked-meat medium and in the blood broth, and on subculture will grow on blood-agar plates incubated under ordinary atmospheric conditions, although much better growth is obtained if the plates are incubated in an atmosphere containing an increased amount of carbon dioxide (Nye and Lamb<sup>30</sup>). Most strains of the last organism are beta hemolytic on blood agar and they are closely related to, if not identical with, the microaerophilic streptococci described by Meleney.<sup>13</sup>

The fusiform bacillus was identified in every patient except the one in whom the infecting organism was *Clostridium welchii*. In only 9 patients were aerobic organisms found, and never were they present without an anaerobe — this in spite of the fact that aerobic cultures were made in every case. These aerobes were the streptococcus, pneumococcus and staphylococcus and the influenza bacillus. Again, it should be pointed out that if aerobic cultures alone were made on all cases, the true nature of the disease might have been overlooked, and the assumption might have been made that the empyema was due to the aerobic organism.

The fusiform bacillus has been described as a strict anaerobe, and many different types have been identified by their morphology alone. Some attempts have been made to distinguish them serologically. The spirochetes have proved to be the most difficult to grow, but they were reported as seen on the direct smear in one quarter of our cases. Four types of the spirochete have been identified by Smith.<sup>26</sup>

### PATHOLOGY

Putrid empyema presents itself as a gangrenous, hemorrhagic pleuritis, with the production of a large amount of fluid and, on occasion, gas. It complicates a gangrenous process of the lung that may be acute or chronic. When the parent disease is acute, there is usually total involvement of the pleura, but when the underlying condition has existed for some time, a moderate amount of walling off may have occurred, and a localized type of empyema then develops. Tissue necrosis is, however, one of the outstanding features of anaerobic infections, hence, the adhesions tend to disappear, and there may result one or more large or small compartments filled with foul pus and debris. The formation of fibrinous adhesions occurs early in every case, and this is an important feature in the treatment of these patients.

The fluid in this disease tends to be thin for a long time, but the pleural reaction is so marked that the mediastinum becomes fixed early.<sup>1</sup> In this series of 90 patients, the fluid was described as thin in 45, creamy in 13 and thick in 24, and was not mentioned in 8. Some patients had a clear serous fluid at the first thoracentesis. Smith<sup>26</sup> has also described this, noting that the fluid may be clear for the first day or so. In the present series, the culture of the clear fluid often showed the anaerobes and the characteristic foul odor was noted. In other cases the fluid was odorless. In 19 cases, the pleural fluid appeared clear on the first thoracentesis, but a second thoracentesis, soon after the first, produced fluid that was both foul and purulent.

The presence of a bronchopleural fistula has frequently been noted in patients with this disease. Its occurrence depends on the underlying disease. The incidence is high in empyema complicating the rupture of a lung abscess, it is medium in the bronchiectasis group and low in the pneumonitis group. In this series a fistula was noted in 25 patients, and may have been present in others, especially in the 19 not operated on. It caused little change in the course of the disease, however, and in all cases closed before there was complete obliteration of the empyema cavity. In 20 cases the fistulas were in the abscess and bronchiectasis groups, and in 2 they were in the tuberculous group.

### ANIMAL EXPERIMENTS

The bacteriologic investigation of putrid empyema by experimental methods has been neglected, but

many investigations of the primary disease have been made, and much of the present discussion concerns these Pilot and Davis<sup>24</sup> were able to show that a pure culture of fusiform bacilli had little pathogenicity In the pleural cavity the organisms caused only a slight fibrinous exudate The cocci — 80 per cent of which were anaerobic streptococci — alone produced a serofibrinopurulent pleuritis without odor When the spirochetes fusiform bacilli and cocci were combined, however, the lesion had a putrid odor Smith<sup>7</sup> has produced pulmonary abscesses, bronchiectasis, gangrene and pneumonia by the intratracheal injection of material from the alveolar border of patients with pyorrhea He demonstrated that four organisms, the anaerobic streptococcus, the fusiform bacillus, a spirochete and a vibrio, were needed None of these alone, nor any mixture without all of them, produced the characteristic lesions

Many others<sup>5, 16, 23, 31-36</sup> have been able to produce these lesions by using the anaerobes, some by the intratracheal route and others by means of infected emboli The material used was generally obtained from the scrapings of the teeth of patients with pyorrhea alveolaris, and was usually shown to contain the anaerobes mentioned above Crowe and Scarff<sup>34</sup> point out the many unsuccessful attempts to produce lung abscesses by the intratracheal inoculation of virulent forms of staphylococcus, streptococcus, pneumococcus and the colon bacillus Yet when the anaerobes were employed, the usual result was a localized chronic pulmonary suppuration

The incidence of empyema is not mentioned in most of the results reported Longacre and Herrmann,<sup>16</sup> however, give the incidence in their experimental series as 10 per cent following the intratracheal method and 33 per cent following the use of emboli infected with anaerobes

METHOD OF INFECTION

Almost all writers agree that there is infection about the mouth in these patients Usually there is pyorrhea alveolaris, chronic ulceration of the mouth or a Vincent's infection Meleney<sup>5</sup> notes that the most frequent anaerobic infections are those about the mouth These organisms may be aspirated, with resulting pneumonitis or abscess and the complication of putrid empyema Duffy<sup>37</sup> was able to show fusospirochetes in all his patients Stern<sup>38</sup> concludes that a thorough investigation of the dental history in cases of abscess of the lung may reduce the percentage of cases formerly grouped as pulmonary abscess of unknown origin He was chiefly concerned with antecedent dental operations, but we have been greatly impressed by the high incidence of unhygienic mouths encountered in patients with putrid empyema without a history of any dental procedure Thus, the taking of alcohol, poor oral hygiene and a period

of unconsciousness prior to the onset of the disease seem to be the usual combination of factors culminating in putrid empyema that is seen in large municipal hospitals Smith<sup>26</sup> also believes that aspiration of infected material from the mouth probably accounts for most pulmonary abscesses, although a small number may be due to emboli from the respiratory passages In this series a description of the teeth was present in the records of 70 patients Of these, the teeth were described as good in 7, as negative in 3 and as showing pyorrhea or chronic infection in 60 This means that at least 85 per cent of the patients had infection about the teeth

CLINICAL FEATURES

Certain clinical features are distinctive of putrid empyema In this series there was a marked predominance of males who comprised 72 of the 90 patients The disease was, however, about equally fatal in both sexes, the mortality being 46 per cent in males and 39 per cent in females

The ages of the patients varied from five to seventy-eight years The relation between age and mortality is shown in Table 3 In general, mortal-

TABLE 3 Relation of Age and Mortality

AGE	No OF RECOVERIES		DEATHS	MORTALITY
	CASES			%
37				
1-9	4	4	0	0
10-19	11	9	2	18
20-29	12	8	4	33
30-39	18	10	8	44
40-49	23	11	11	50 (22 cases)
50-59	9	3	6	67
60-69	7	5	2	29
70 up	6	0	6	100
Totals	90	50	39	

ity increased with age An explanation for the low mortality in the sixty-to-sixty-nine-year group is suggested by the type of surgery employed In this group, 5 of 7 patients recovered and all of these, and only these, had adequate surgery This indicates that the other patients in the older age groups were deprived of the chance that adequate surgery might have offered In many cases the records showed that there had been much waiting for the patient's condition to improve, whereas it deteriorated rapidly and progressively The condition on admission was said to be poor in 42 patients, fair in 27 and good in 15 The condition of 6 patients was not recorded In other words, most of the patients appeared to be acutely ill at the time of admission Their poor general condition is not an accurate indication for delaying surgery, on the contrary, it suggests that immediate surgery is imperative

Although the disease evolves in a variety of ways, there are some constant signs A frequent complaint is severe pain, often localized, and persisting even after the development of fluid Associated with this is a localized tenderness of the chest wall, which is a frequent indication of severe gangrenous



infections of the pleura. The clinical impression on admission in many patients was that of pneumonia, usually based on a history of pain in the chest, chills and cough, yet the physical signs were those of fluid, which characteristically develops early in the disease.<sup>2</sup> The roentgenogram was occasionally misleading, showing consolidation even when fluid was present. A history of cough of long duration, often with foul sputum, was frequent and was helpful in making the diagnosis.

These patients are often far more ill than one would expect from the amount of discoverable disease. They early become toxic and delirious. They frequently show signs of peripheral vascular collapse, with cold, clammy extremities and an extremely rapid pulse. The temperature, although elevated, is not in proportion to the pulse, a feature common to all anaerobic infections.

The diagnosis of this disease is made by thoracentesis. Fluid having a foul odor is pathognomonic, although a direct smear that reveals the fusospirochetes is corroborative evidence, easily obtained. Anaerobic culture of the fluid must be done, for aerobic culture does not reveal the true nature of the infection. In reviewing these cases, it was not unusual to find that two or more aerobic cultures had been done without growth before an anaerobic culture revealed the infecting organisms. Purulent chest fluids should always be cultured anaerobically, especially those that are foul.

One complication of thoracentesis, cellulitis of the chest wall, has been noted by many authors.<sup>1, 2, 17, 18</sup> It is so grave that every precaution should be taken to circumvent its occurrence. Apparently the thin, watery fluid easily passes along the needle track into the deep tissues of the chest wall. There, under the muscles, in the tissues overlying the ribs, conditions are ideal for the growth of anaerobes. Severe pain and tenderness soon appear. Within twenty-four hours there is marked redness, and a cellulitis with gangrene of the deep tissue rapidly develops. Because of this, most observers have wisely stated that thoracentesis should be followed by surgery as soon as possible and that repeated thoracenteses are contraindicated. It is true that in some patients thoracentesis can be done more than once without this complication, on the other hand, when it develops it is of such severity that it approaches in importance or overshadows the underlying disease.

Maier and Grace<sup>1</sup> encountered cellulitis of the chest wall in 4 of their 23 patients, despite the fact that about half the patients were operated on within twenty-four hours of the thoracentesis. In the present series, 21 patients developed this complication. If those operated on within twenty-four hours are eliminated, 38 per cent developed it. In our experience this complication is so severe and frequent that we, too, believe that thoracentesis should be done only for diagnostic purposes and

should be immediately followed by open drainage. Also, because this complication may develop, closed thoracotomy or the suture of wounds after rib resection is extremely hazardous.

### TREATMENT

The rate of recovery is greatest in the patients operated on early. The average of the time intervals from the onset of the disease — calculated as accurately as possible from the records — to the time of operation in those who lived was 5.2 days, and in those who died it was 10.7 days. This may be expressed in another way by considering all the patients who had surgical treatment. On the first to the third day, 25 patients were operated on and 22 recovered, a mortality of 12 per cent. On the fourth to the seventh day, 22 were operated on and 16 recovered, a mortality of 27 per cent. On the eighth to the tenth day, 13 were operated on, and only 6 recovered, a mortality of 54 per cent. Hence, it can be seen that 75 per cent of the patients who were operated on in the first week of their disease recovered, whereas slightly more than one third of those who died were operated on within the first week. Further evidence of the need for early surgery can be obtained from the fact that of the 18 patients who died without operation, 10 did so within the first ten days of their disease. In 7 cases, it was impossible to calculate the exact duration of the disease with any accuracy, but in most of the cases the course was probably less than ten days. Only 1 patient lived with the disease over the ten-day period.

With few exceptions there is unanimity of opinion on the treatment of this disease. All writers agree that surgery is indicated and that open drainage is the treatment of choice. Graham, Singer and Ballou<sup>4</sup> believe that it is safer to aspirate frequently or to use closed drainage, and give as their reasons those that generally pertain to pyogenic empyema. Flack<sup>3</sup> thinks that conservative treatment with an intercostal tube and later resection of a rib is the treatment of choice. The differences of opinion on the treatment of the disease depend largely on the question of mediastinal stabilization. If one applies the usual principles that govern the treatment of postpneumonic empyema and awaits thickening of the purulent fluid to the consistence at which mediastinal fixation may be postulated, valuable time may be lost.

The sole attribute common to all anaerobes is their inability to multiply or even live in an atmosphere rich in oxygen. It has been shown that they succumb after only a few hours of contact with oxygen, even in low concentration. Consequently, most writers have agreed that open operation with adequate aeration and evacuation of the pus is the best treatment.

Moreover, in this disease, despite the consistence of the fluid, there is prompt stabilization of the

mediastinum, so that early operation may be accomplished. Maier and Grace<sup>1</sup> noted that all except one patient in their series with thin fluid had a fixed mediastinum.

In 1938, Dolley and Jones<sup>39</sup> described a method for open drainage of acute pyopneumothorax in patients in whom the mediastinum is not stabilized. This procedure is simple and logical and has proved most successful in our patients. It is to be remembered that the cases causing concern about the stability of the mediastinum are few, for, as has been noted, early fixation is the rule. The method to be described provides an adequate method of treatment in the event that a mobile mediastinum is encountered. With this method none of our patients developed chronic empyema, and the average time of treatment from operation to complete closure of the wound was seven weeks. Another type of treatment which agrees with ours in principle but differs slightly from it in technic, is that described by Sauerbruch and O'Shaughnessy.<sup>29</sup> This consists in the removal of two dependent ribs under positive-pressure anaesthesia and open packing of the wound.

#### *Operative Technic*

The operative method that we have used follows closely that of Dolley and Jones,<sup>39</sup> described for the treatment of acute pyopneumothorax following the rupture of a lung abscess. We have used 1 per cent procaine infiltration as the anesthetic of choice. A 20-cm incision is made over the most dependent rib, as determined by thoracentesis, and is extended from the posterior to the anterior axillary line. It is carried through the muscles, and a segment of the appropriate rib as long as the incision is resected subperiosteally in the usual fashion. A large dressing has already been prepared for immediate use.

From this point the procedure is determined by the degree of mediastinal fixation. This may be judged by the amount of pleural thickening or by means of a small incision into the pleural cavity. If there is inadequate fixation, the pleura is quickly incised the entire length of the incision, the dressing is applied, and the patient is quickly turned on his back. With this routine rapidly performed, the dangers of open pneumothorax are largely circumvented, for the dressing soon becomes saturated and serves as a tampon, preventing the exchange of air through the wound, yet the wide opening thus secured allows complete drainage into the dressing. The dressing is not changed until the third day, when a quick change is made. Stabilization usually occurs from the fifth to the seventh day, and from then on a tube or pack can be used. It has been our policy to use a gauze pack impregnated with activated zinc peroxide, placed partly in the pleural cavity and partly in the wound. By this means the odor disappears and the wound is

clean and granulating five to seven days after the treatment is begun. Tubes are then inserted. The convalescent treatment is the same as that for the usual postpneumonic empyema. The use of zinc peroxide has been found of value by many others in anaerobic infections,<sup>1, 3, 17, 40</sup> and we cannot emphasize its value too strongly for this type of disease.

If the fixation is adequate, more time can be spent examining the cavity and removing all the pus and fibrin by suction. Otherwise, the treatment is the same, except that the zinc peroxide is used from the time of operation.

Under no circumstances is an attempt made at any type of wound approximation, and hemostasis is obtained with a minimum of ligatures.

Most of the patients so treated show immediate improvement. In a few days the appetite returns and they become more active in bed. For a considerable period, often two or three weeks, however, these patients have a low-grade fever apparently due to the primary intrapulmonary infection. Irrigations are not always possible because of the existence of a fistula. If one is not present, irrigations may be helpful because of their mechanical cleansing action.

#### *Drug Treatment*

The effect of the sulfonamides on the anaerobes is still uncertain. Some evidence has appeared that these drugs are of no value in this type of infection, but this is confusing and uncertain. Meleney<sup>5</sup> believes that their value in this type of infection, in which there is early destruction of tissue, has not been demonstrated. Maier and Grace<sup>1</sup> found that the typical dramatic response to these drugs did not occur in this type of infection. In fact, they believe that this failure of response is a point of differentiation between the atypical pneumonia associated with foul empyema and the typical pneumococcal pneumonia.

Twenty-one of the patients in this series were treated with one of the sulfonamides—usually sulfathiazole or sulfapyridine. Of these, only 1, with an infection due to *Cl. welchii*, showed a favorable response. We are of the opinion that these drugs are of no benefit once the empyema has developed, regardless of what value they may prove to have for the primary disease. The other drugs ordinarily used in fusospirochetal infections are the arsenicals. Despite any questionable value they may have for the primary disease, they are of no worth in the treatment of putrid empyema.

We have treated recently 2 cases of putrid empyema, not included in this series, by the intramuscular and intrapleural injection of penicillin. In the first case the empyema complicated a pneumonia that was apparently the result of the aspiration of infected material from the mouth. The pleural fluid was typically putrid, and cultures re-

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SUMMARY

Putrid empyema is shown to be a distinct disease entity differing in its etiology, bacteriology, pathology and clinical aspects from postpneumonic or other pyogenic empyemas

Bacteriologically, the disease is due to certain anaerobes that produce a gangrenous sloughing pleuritis Clinically, it is characterized when untreated as an acute onset followed by a rapid severe course and an early fatal termination

The fact is stressed that in many patients the fluid is thin for some time This characteristic should be noted but should not be considered a criterion in treatment Concern about the consistence of the fluid is fatal, for it is a frequently noted fact that stabilization of the mediastinum occurs early in these patients If the mediastinum is not stabilized, patients can be operated on by the method herein described and thereby receive the benefits of early and open operation

A review of the 90 cases reported demonstrates the value of early open operation Zinc peroxide is of distinct value in postoperative treatment Once the foul odor has disappeared and the hazard of open pneumothorax is in abeyance, these patients may be treated like those with the ordinary pyogenic empyema

Further experience may show that penicillin is a valuable adjunct in the treatment of putrid empyema

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vealed the usual mixed flora. Twenty-five thousand units of penicillin was daily administered intrapleurally for ten days, a total of 250,000 units. Following this the fever persisted, and five days later rib resection was performed, with the intention of draining a residual pocket. Exploration revealed only fresh adhesions and a thickened pleura. The chest was closed without drainage, and the patient made an uneventful recovery.

In the second case the empyema complicated a pneumonitis that resulted from the post-partum aspiration of vomitus or mouth secretions or both. The patient was considered moribund when first observed. She received 10,000 to 60,000 units of penicillin intrapleurally daily for fourteen days, a total of 368,000 units. During that time there was striking improvement in the general condition. On the fifteenth day, rib resection was performed for the drainage of a localized empyema. The patient also received an average of 120,000 units of penicillin intramuscularly daily for thirty-nine days, a total of 4,640,000 units. A lung abscess that developed in the upper lobe at the site of the original pneumonitis was drained in two stages on the thirtieth and thirty-sixth days. The patient was discharged on the seventy-fourth day, the temperature having been normal for fifteen days. She has been well for over a year.

One may conclude that penicillin is a valuable adjunct in the treatment of putrid empyema and effects cures in a certain percentage of cases.

### RESULTS

Tables 4 and 5 show the results of treatment in this series. The former includes the total series of patients, whereas the latter records only those who were treated on the Thoracic Surgery Service. In explanation of these tables, "rib resection" refers to the usual type of operation done for empyema,

TABLE 4 *Results in the Total Series*

TYPE OF TREATMENT	NO OF CASES	RECOVERIES	DEATHS	MORTALITY %
No operation	19	0	18	100 (18 cases)
Closed thoracotomy	13	2	11	85
Rib resection	31	25	6	19
Open resection	22	19	3	14
Combined closed and open thoracotomy	5	4	1	20
Totals	90	50	39	

with wound closure about one or more tubes. "Open resection" refers to the method described herein, with wound left widely open.

If one first considers the mortality for each type of operation, one sees clearly the value of the adequate types of surgery as represented by rib resection and open resection. The results with the conventional rib resection were good, and the insertion of tubes may be helpful, if there is time. We believe, however, that the use of zinc peroxide is specifically so valuable that it is better to wait until the anaerobic infection has cleared, as judged by the foul

odor, before using the tubes. Finally, closure of the wound is of no value and may cause definite harm in some patients, for in this series one third of the patients whose wound was sutured developed

TABLE 5 *Results in Patients Treated on the Thoracic Surgery Service*

TYPE OF OPERATION	NO OF CASES	RECOVERIES	DEATHS	MORTALITY %
Closed thoracotomy	2	0	2	100
Rib resection	9	6	3	33
Open resection	21	18	3	14
Combined closed and open thoracotomy	2	2	0	0
Totals	34	26	8	
Average				23

a gangrenous, sloughing wound infection, with associated necrotizing phlegmon and eventual complete dehiscence.

These results demonstrate the benefit of immediate surgery of the open type. The 2 patients on the Thoracic Surgery Service who had a closed thoracotomy were seen late, when they were suffering the combined effects of overwhelming sepsis and severe tension pneumothorax, with marked mediastinal displacement. The closed thoracotomy was done immediately as a temporizing measure, but the patients died soon after it, before more could be done. It is doubtful that any type of operation would have helped one of these patients who had extensive bilateral pulmonary tuberculosis.

The results of combined surgery — that is, closed and open thoracotomy — appear to be good, but in both patients on the Thoracic Surgery Service the closed drainage represented a temporizing measure done immediately to correct altered chest mechanics and to allow time for general treatment. In both cases, open resection was done very shortly after the tube drainage. In the other 2 recovered patients who had combined surgery in the total series, both had closed drainage for many months, which proved to be inadequate and had to be followed by rib resection for adequate drainage. In 1 case, however, a chronic empyema resulted.

The 3 deaths among the 21 patients receiving open resection indicate that the mortality when treatment is adequate is usually from the primary disease. One patient died from multiple acute lung abscesses, which had been progressing when the empyema developed. The second died from a gangrenous pneumonitis involving the entire left lung and the lower right lobe. The empyema was on the left, and drainage was accomplished without incident. One week after the drainage, however, spread of the intrapulmonary disease to the right side occurred, and the course was downhill thereafter. The third patient, who had extensive intrapulmonary disease, died twenty-two days after the drainage of a brain abscess, although the empyema was healing well.

## SUMMARY

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The fact is stressed that in many patients the fluid is thin for some time. This characteristic should be noted but should not be considered a criterion in treatment. Concern about the consistence of the fluid is fatal, for it is a frequently noted fact that stabilization of the mediastinum occurs early in these patients. If the mediastinum is not stabilized, patients can be operated on by the method herein described and thereby receive the benefits of early and open operation.

A review of the 90 cases reported demonstrates the value of early open operation. Zinc peroxide is of distinct value in postoperative treatment. Once the foul odor has disappeared and the hazard of open pneumothorax is in abeyance, these patients may be treated like those with the ordinary pyogenic empyema.

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## THE EARLY DIAGNOSIS OF MINIMAL PULMONARY TUBERCULOSIS\*

I D BOBROWITZ, M D,† AND RALPH E DWORK, M D ‡

OTISVILLE, NEW YORK

THERE are numerous vital reasons that indicate the importance of diagnosing tuberculosis in the minimal stage. The results of sanatorium treatment and follow-up analyses many years after discharge have uniformly shown the following constant and unequivocal advantages for minimal cases in comparison with advanced tuberculosis.<sup>1-4</sup> The percentage of arrested or healed cases is highest, and the time required to obtain an arrest of the disease much the shortest in minimal cases. This group also has the smallest incidence of instability. Collapse measures are infrequent and when used are less extensive, with complications, morbidity and mortality thereby reduced. The sputum is not so often positive as in moderately and far advanced cases. This is important, for all therapeutic procedures aim at the reversal of a positive to a negative sputum. The great majority of patients with persistently positive sputums sooner or later progress and have a bad prognosis, with little chance of survival. During the institutional and follow-up phases of treatment, the number of deaths are markedly less in cases diagnosed in the minimal stage than in those found with advanced tuberculosis, and the patients live much longer. The need for patients to be readmitted after discharge from the sanatorium increases as the stage of the disease advances. The minimal cases, moreover, have far fewer recurrences. All follow-up studies also show that the percentage of those employed or able to work is much higher in this group.

There are great benefits to the public in the early diagnosis and cure of the disease. The spread of tuberculosis from persons with positive sputums to their families and friends and the community is avoided, and a health hazard of first importance is controlled. The shorter hospitalization period required for minimal cases means that cure is effected at a lower cost. Furthermore, these patients often adjust themselves economically, and public expenditures for them and their families are thereby definitely lowered.

The practicing physician is an extremely valuable case-finding agent, since he is in a position to discover a vast number of persons with tuberculosis. Indeed, a large portion of patients see him before anyone else. These opportunities for diagnosis are particularly significant at this time, since war, as always, has increased the incidence of tuberculosis.

To determine the factors that could aid the making of an early diagnosis, 200 cases with minimal lesions

were studied. These patients were consecutive admissions to the sanatorium, and all the cases were minimal on admission, according to the standards of the National Tuberculosis Association.

Of the entire series, 155 patients were between the ages of fifteen and thirty-five. Forty-five patients were over thirty-five years old, with 20 of them older than forty. There has not been enough emphasis on the fact that tuberculosis often occurs in the elderly. Older people represent a great source of infection, for far too frequently their symptoms are explained on the basis of other conditions, such as a chronic bronchitis, asthma or winter or cigarette cough. The 200 patients were quite evenly distributed according to sex—96 males and 104 females. One hundred and one were single, 86 were married, and 13 had separated or been divorced. Of the entire group 123 were Whites, 52 were Negroes, 5 were Chinese, and 1 was a Filipino. Over forty different occupations were represented. These personal data indicate that tuberculosis should be suspected at any age and in any occupation. They may also have any type of social or economic background.

One hundred and thirty-three patients had no specific contact history. Fifty-seven had had definite close association with tuberculosis, 7 had had slight contact, and 3 had had possible exposure. In other words, 67 patients (34 per cent) had had some contact with tuberculosis.

A history of contact with this disease is significant mainly in its indication that the patient has had opportunities to become infected. In fact, many more cases are found in these persons than in the general population. The high tuberculosis morbidity and mortality rate for those with a history of household contact has often been emphasized and the particular danger for children has also been stressed.<sup>5, 6</sup> Every person who has had contact with tuberculous patients should have a complete examination, including x-ray, at once. This should be repeated every year, and preferably every six months. As our figures show, however, lack of contact does not rule out the presence of tuberculosis.

Of these 200 patients, only 37 (19 per cent), were without symptoms. One hundred and fifty-five patients had specific complaints, and 8 gave a history of pleurisy. All the patients had symptoms before or at the time of diagnosis except 6 who developed them after diagnosis. Table 1 lists the symptoms and the number of patients in whom they were present. These symptoms may also be classified according to the body system involved. Pulmonary symptoms comprised 44 per cent, con-

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stitutional or general symptoms, 36 per cent, pleural symptoms 12 per cent, gastrointestinal symptoms 4 per cent, and laryngeal, bone and joint, nervous system, genitourinary, nasopharyngeal and lymphatic system each 1 per cent or less

The statement has often been made that minimal tuberculosis is asymptomatic. This study significantly shows that the great majority of these patients

TABLE 1 *Distribution of Symptoms \**

SYMPTOM	NO. OF CASES
Cough	98
Expectoration	70
Loss of weight	68
Chest pain	61
Weakness (fatigue or lassitude)	55
Fever	28
Hemoptysis	24
Night sweats	24
Streaking	18
Dyspnea	15
Anorexia	13
Chills	9
Hoarseness	6
Irritability	3
Low-back pain	3
Joint pain	3
Diarrhea	2
Headache	2
Insomnia	2

\*There were single cases of the following complaints: amenorrhea, polyuria, cervical node enlargement, nasal discharge, sore throat, spine pain, constipation, dysphagia, nausea, abdominal pain, melena, rectal sinus discharge, dizziness, laryngeal pain and orthopnea.

do have symptoms. Practically all the symptoms in our patients were unquestionably associated with the tuberculosis. It may be argued that sanatorium patients are symptom-conscious. We believe that complaints actually exist, and a careful history and close questioning of the patients will verify this fact. Frequently only after a diagnosis has been made by routine roentgenography does the patient realize that he has symptoms. This is because the symptoms are not often those of a startling character, such as hemoptysis, blood-streaking of the sputum or pleural pain, but instead are those not arresting in nature, such as cough, — usually explained as due to cigarettes, — fatigue or slight loss of weight. The patients usually consider these of minor importance. These beliefs are substantiated by the experience in the 91 patients in whom a diagnosis was made by routine examination (90 by x-ray and 1 by fluoroscopy), 55 (60 per cent) of whom had symptoms. Abeles and Pinner<sup>7</sup> observed 91 patients whose tuberculosis was accidentally discovered on routine examination. Of this group, 28 cases were minimal, and 89 per cent of these patients had had symptoms at some time.

Certain symptoms are particularly frequent in minimal tuberculosis. Unfortunately, however, these are not characteristic or specific for this disease alone. They may be present in nontuberculous lung or pleural lesions or even in nonpulmonary conditions. Symptoms in themselves, therefore, cannot serve as the sole criterion for the diagnosis of tuberculosis, but when present they should

definitely suggest the disease, and the diagnosis can then be made only by following through with a chest x-ray examination.

Besides contact and routine examinations, the only factor that aided early diagnosis in this series was an acute onset or hemoptysis that prompted an immediate medical checkup. On the other hand, delays in diagnosis were seen because of noncooperativeness in the patients. This was usually due to their failure to seek medical advice early, but occasionally a contact neglected to undergo the examination recommended by the physician. There is much need for education of the public to consult physicians early regarding symptoms. The importance of the symptoms should be stressed, especially those that are not striking in character, which have too often been considered trivial.

In 21 patients a diagnosis of tuberculosis was not suspected or made at the first medical consultation or examination. If the 91 patients diagnosed routinely are not considered, this means that 21 of 109 patients (19 per cent) were missed. The mistaken diagnoses included the following conditions: pneumonia, 3 cases, pleurisy, 3 cases, asthma, 3 cases, "cold," tonsillitis, and dyspepsia and colitis, 2 cases each, and influenza, sinusitis, nephritis, rheumatic heart disease, arthritis and unexplained fever, 1 case each.

Almost 75 per cent of the errors were in diagnoses of nontuberculous respiratory or upper respiratory conditions. To prevent these errors, it should be a routine practice not to make a diagnosis of pneumonia, bronchitis, asthma, pleurisy, chest cold, catarrhal fever or grippe without first considering the possibility of tuberculosis. The symptoms and physical findings in these cases may be the same as those encountered in tuberculosis. To determine definitely the presence of tuberculosis an x-ray and sputum examination and occasionally a tuberculin test are requisite for all these patients. This would not be an impractical or uneconomical procedure, for the yield of active cases of tuberculosis would be considerable.

The most valuable diagnostic physical finding in tuberculosis is the presence of rales. Changes in fremitus, dullness and breath sounds are not significant enough to be considered. Only 57 (29 per cent) of these 200 minimal cases had rales. This shows how unreliable a physical examination is in the early diagnosis of tuberculosis. A lack of physical signs cannot rule out the disease, for in minimal tuberculosis a normal physical examination is usual.

In 156 patients no tubercle bacilli were recovered, in 3 the records contained no reports, the patients having left the sanatorium before examinations could be made, and in 41 tubercle bacilli were found. They were reported either in smears of the sputum or gastric contents concentrates or in cultures or both. The demonstration of tubercle bacilli is,



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Bloch and Tucker<sup>11</sup> have affirmed the value of fluoroscopy. They found tuberculous lesions of the reinfection type in 4.1 per cent of 15,000 clinic patients. Of these cases, 1.4 per cent were clinically significant and 58.6 per cent were minimal. These authors stress the following points. The fluoroscope is easy and economical to operate and is extremely adaptable to the practicing physician's office. Its routine use would be a significant diagnostic contribution. It has additional value because an ordinary film may miss a lesion hidden by the scapula, clavicle, ribs or heart, whereas with the fluoroscope the patient can be rotated and the clavicles elevated or depressed.

Daniels<sup>12</sup> emphasizes that the physician in general practice can be an extremely valuable case-finding agent, and considers the large group of patients that come to physicians' offices a fertile field for mass surveys. He estimates that 30 per cent of the general population visit a physician at some time during the year. He reports a study wherein every patient entering his office, irrespective of the complaint, was fluoroscoped and x-ray photographs were taken of all chests with suspicious lesions. In 250 patients, 7 active cases of pulmonary tuberculosis were found. Of these patients, none had a history of contact, 4 had positive sputums, 6 had no physical findings, 3 had an increased sedimentation rate, and 5 had no history indicating pulmonary disease. Daniels admits the errors of fluoroscopy, and advocates having an x-ray miniature-film machine available in each locality for examining all patients visiting private physicians. Fluoroscopy is of definite value and is much better than a physical examination for the discovery of minimal cases, but it is imperfect and cannot be relied on solely for diagnosis. To be certain of the presence or absence of tuberculosis, it would be necessary to x-ray patients considered negative on fluoroscopy.

X-ray examination was the main method employed in diagnosis, having been used in 187 (94 per cent) of the 200 cases in this series prior to admission to the sanatorium. In 97 of these, the film was utilized in a corroborative manner to determine the presence of tuberculosis suspected because of other factors — symptoms, physical

findings and so forth. In 90 cases, the examination was routine consisting of a contact examination, survey, pre-employment investigation or a Selective Service checkup and the diagnosis was made in persons apparently healthy.

The main problem in the control of tuberculosis is that of early diagnosis. In addition, treatment that is necessary should be provided without delay, either in the home, if the conditions there are suitable, or in an institution. The physician has the duty to educate the patient and his family in the infectiousness of the disease and to convince them of the value and necessity of immediate care. A patient may delay proper attention at home, postpone seeking admission to the sanatorium or continue to work after the diagnosis because necessary home adjustments, such as adequate living arrangements, placement of children, payment of rent, purchase of food and clothing, storage of furniture, contact examinations and family medical care, have not been made. To meet these situations requires the co-operation of public or voluntary social-service and welfare associations and of public-health nursing and medical groups. If such problems are taken care of, patients will be prompted to accept medical treatment as soon as the diagnosis has been made. The possibility of progression of the disease can then be avoided and the morbidity and mortality of advanced tuberculosis thereby avoided.

#### COMMENT

This study has shown that the most important and reliable instrument in the early diagnosis of minimal tuberculosis is x-ray examination. Certainly in over 99 per cent of minimal cases it can effect the diagnosis, often long before other clinical or laboratory findings have indicated the disease. No lung examination can be considered complete without an x-ray examination, and a patient should never be told that tuberculosis is absent unless one has been done. This procedure should be employed in every patient with any symptoms suggestive of tuberculosis, in any illness that tuberculosis may simulate and periodically in all contact cases. Minimal tuberculosis is a symptomatic disease, but to diagnose all persons, including those in an asymptomatic phase, routine mass x-ray surveys are necessary.

Ninety-one (46 per cent) of the patients in this series were diagnosed on a routine examination, — 90 by x-ray and 1 by fluoroscopy — indicating the value of routine investigation. These were apparently healthy persons unsuspected of having an illness, in whom the tuberculosis was accidentally discovered through x-ray examination. Without this fortuitous circumstance, many patients would no doubt have eventually been diagnosed as advanced cases. That routine x-ray surveys find active minimal lesions is an established fact. Of

of course, absolute proof of tuberculosis, but the presence of a negative sputum does not mean that tuberculosis is absent. This is particularly true in minimal cases, as illustrated by the small percentage in this series without positive sputums. A more liberal use of cultures and utilization of guinea-pig inoculations would, however, have yielded a higher percentage of positive reports.

There are several important facts relative to the finding of tubercle bacilli. The number of positive reports depends on the frequency and manner of examination. A single sputum, if negative, is of no value in the diagnosis of tuberculosis. The longer the time used for the collection of sputum, the higher is the incidence of a positive sputum. The use of sputum concentrates alone is not satisfactory; fasting gastric contents must also be examined. This is essential whenever sputum concentrates are negative or there is little or no expectoration. Especially in minimal cases, little sputum may be raised or, as often occurs, the sputum may be swallowed. Sputums or gastric contents that are negative on concentration should be cultured, for many will thus be found to be positive. Moreover, repeated examinations are necessary for proper conclusions about the presence of tubercle bacilli. Should the findings still be negative and tuberculosis be suspected, guinea-pig inoculations of the sputum and gastric contents are required. The ascending order of sensitivity of the methods used in finding tubercle bacilli is as follows: direct smear, 24-hour sputum concentrate, 72-hour sputum concentrate, fasting gastric contents concentrate, culture of sputum or gastric contents and guinea-pig inoculations. The comparison of the sensitivity of these tests has been described.<sup>8, 9</sup> In the 41 cases in which tubercle bacilli were found, 10 (24 per cent) were positive with sputum or gastric cultures alone, 9 (22 per cent) with gastric concentrates alone, and 4 with gastric concentrates combined with sputum and gastric contents cultures. In other words, in 56 per cent of the patients with tubercle bacilli, they were revealed because of the examination of gastric contents and the utilization of cultures. Decker, Ordway and Medlar<sup>9</sup> report that the repeated use of cultures and guinea-pig inoculations of sputum and gastric contents disclosed bacilli in 70 per cent of active minimal cases.

It is not meant by this discussion that it is necessary to wait for a positive sputum to make a diagnosis of minimal tuberculosis, since an early x-ray examination will indicate the disease. Needless to say, in a case with a purulent sputum persistently negative for tubercle bacilli, tuberculosis is undoubtedly not present.

Other laboratory findings were of little help in diagnosis. The white-cell count was of negligible value. On admission to the sanatorium 148 patients had a count under 10,000, 25 had counts between 10,000 and 15,000, and only 1 patient had a count

of more than 15,000. In 26 cases no count was available.

The sedimentation rate, although more sensitive than the white-cell count, was not diagnostic or indicative of clinical activity. Of the 200 patients, 89 (45 per cent) had a sedimentation rate of less than 10 mm in one hour (Cutler method), 42 patients had a rate of 11 to 15 mm, 29 had a rate between 16 and 20 mm, and 40 had a rate over 21 mm, with all but 2 of these under 30 mm. Thus, 111 (56 per cent) of the patients had a sedimentation rate of over 10 mm.

The tuberculin test was apparently not used in the diagnosis of any patient, but it is possible that in some cases the procedure was carried out without being recorded.

A positive tuberculin reaction means only that a tuberculous infection has taken place in the body, with hypersensitivity to tuberculo-protein present. It provides no definite answer about the type, extent or activity of the disease. A negative reaction may occur in the presence of tuberculosis under special circumstances — if the test is done shortly after infection has taken place and before the tissues have become hypersensitive, in terminal tuberculous disease, in patients with healed tuberculous lesions, in intercurrent acute infections and in aged and debilitated persons. The percentage of reactors is also qualified by the amount of tuberculin, for the larger the dose the greater the number of positive cases. A maximum final dose of 10 mg is required for definite conclusions, since a negative reaction with so much tuberculin usually rules out tuberculosis. The test is especially significant in infants and young children, for if the reaction is positive, it constitutes strong evidence of active tuberculous disease. Rechecking a negative case periodically sometimes shows a positive reaction, thus indicating the occurrence of tuberculous infection. The important point is that the tuberculin test used alone for diagnostic purposes misses many minimal cases, particularly in adults, and that x-ray examination is essential to make the diagnosis.

Fluoroscopy was recorded in 8 cases (4 per cent). In 7 of these it served as a corroborative measure in suspected cases of tuberculosis, and in 1 case it formed a routine examination in an apparently healthy person. This figure is probably not a true indication of the use of the fluoroscope in diagnosis, since the patients no doubt were not specifically questioned about it.

There have been divergent opinions concerning the value of fluoroscopy as a method of early diagnosis. Garland<sup>10</sup> has emphasized the following limitations of this procedure. Its efficiency depends to a moderate degree on the technical factors, and to a high degree on the time taken by the examiner to get his eyes accommodated to the fluoroscope. There is much variation in the visual acuity of physicians. Fluoroscopy is much less accurate than

radiography, even when carefully done by trained persons. Published studies of fluoroscopy and roentgenographic checkups show that in the hands of experts errors vary from 13 to 35 per cent. The highest number of errors occur in minimal cases, especially those with apical or supraclavicular lesions. Fluoroscopy is especially difficult in obese, thick-chested patients. From the viewpoint of economy, it actually does not cost much less than x-ray examination if allowance is made for the physician's time required for eye adaptation, examination, discussion and a report of the case. Moreover, the cost of missed cases is greater than the cost of x-ray examination.

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these 91 patients, 55 had symptoms, 21 were shown to be positive for tubercle bacilli, and 38, including 14 with progression, showed x-ray changes

The greatest advance in tuberculosis in recent years has been the lesson taught by the mass x-ray surveys. These surveys, applied to Selective Service applicants, to the industrial population, to those to be employed, to those admitted to general hospitals and so forth, have found evidences of clinically significant pulmonary tuberculosis of reinfection type in at least 1 per cent of the cases. Most important is the fact that 65 per cent of the cases have been diagnosed in a minimal stage. The statistics of the surveys indicate that there are many hundreds of thousands of unrecognized and unsuspected cases of tuberculosis in the country that can be detected by routine x-ray examinations. Moreover, rapid, simple, economical and diagnostically accurate methods have been developed, through the use of 14-by-17-inch paper films and 4-by-5-inch and 35-mm — and recently 70-mm — miniature films taken with photofluorographic technique. The routine use of x-ray examination is not an impractical ideal but an absolute necessity and a judicious economy. There is a much greater cost — to the patient, his family and the public — in a missed or delayed diagnosis of tuberculosis than in the expenditure for films that reveal no lesions. It is hoped that in the near future the means will be found to arrange for routine and periodic radiographic examinations of the entire population of the country. When this is done, a great step forward will have been taken in the early diagnosis and eradication of tuberculosis.

#### SUMMARY AND CONCLUSIONS

The advantages of the early diagnosis of minimal tuberculosis are enumerated.

To determine the factors that could aid early diagnosis, 200 cases with minimal lesions have been studied and the results reported.

Tuberculosis should be suspected at any age, in any occupation and with any type of social or economic background.

Positive contact is not a clear diagnostic indication and was present in only 34 per cent of the patients. Close observation is, however, necessary for contact cases, since the incidence of tuberculous infection among them is high.

Minimal tuberculosis is a symptomatic disease. Eighty-two per cent of these patients had symptoms. This is contrary to the oft-repeated statement that minimal tuberculosis is asymptomatic. The complaints usual in tuberculosis are either acute or

not arresting. The public should be taught the importance of symptoms.

Minimal tuberculosis can masquerade as one of many other ordinary illnesses.

Physical findings are totally unreliable in diagnosis. Only 29 per cent of the patients in this series had rales.

Tubercle bacilli were found in 21 per cent of the cases. The percentage of positive reports depends on the type and number of examinations. Sputum smears alone are of very little value. Concentrates and cultures — and ideally guinea-pig inoculations — of sputum and fasting gastric contents are required for an adequate search for tubercle bacilli.

The white-cell count and sedimentation rate are of little diagnostic help.

The tuberculin test received almost no use in the diagnosis of these cases.

Fluoroscopy has its value but is an imperfect diagnostic method.

The vital role of the practicing physician as a tuberculosis case-finding agent has been indicated.

Prompt acceptance by patients of medical treatment is essential.

X-ray examination was used for diagnosis in 94 per cent of the cases before admission. This is the only reliable method for early diagnosis of minimal tuberculosis. Films should be taken in every case with symptoms suggestive of tuberculosis, in any illness that may be tuberculosis and periodically in all contact cases. Routine radiographic examinations are required for the entire population. The value of mass x-ray surveys has been demonstrated.

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## PENTOTHAL SODIUM ANESTHESIA IN NEUROLOGIC SURGERY

EDWARD W. SHANNON, M.D.,\* AND W. JAMES GARDNER, M.D.†

CLEVELAND, OHIO

THE purpose of this article is to summarize our experience with Pentothal Sodium anesthesia in neurologic surgery. Since this kind of anesthesia was first used in this clinic for pneumoencephalography,<sup>1</sup> its use has been extended to include all

## PREOPERATIVE PREPARATION

The night before operation a cleansing enema and 0.1 gm of Seconal Sodium are given. The meal before operation is omitted and 0.1 gm of

TABLE 1 Summary of Data

FACTOR	TYPE OF OPERATION							TOTALS
	SUPRATENTORIAL CRANIOTOMY	SUBOCCIPITAL CRANIOTOMY	SECTION OF FIFTH SENSORY ROOT	LUMBAR LAMINECTOMY FOR PROTRUDED INTERVERTEBRAL DISK	DORSAL SYMPATHETOMY	LAMINECTOMY FOR CORD TUMOR OR CERVICAL DISK	MISCELLANEOUS*	
	30 Cases	11 Cases	21 Cases	10 Cases	6 Cases	6 Cases	17 Cases	
Age incidence (years)								
11-20	2	1			1		2	6
21-30	5	3		1		1	4	14
31-40	9	2	2	2	4	2	6	27
41-50	5	3	3	5	1	2	4	23
51-60	8		7	2		1	1	19
61-70	1	2	6					9
71-80			3					3
Duration of anesthesia (hours)								
1/2 or less			7					7
1/2-1	2	2	11	6			10	31
1-1 1/2	10	2	3	3	2	3	2	25
1 1/2-2	7	2		1	3	2	3	18
2-2 1/2	3	4			1	1	2	12
2 1/2-3	3	2						5
3-3 1/2	3							3
Dosage of 2.5% Pentothal Sodium solution (cubic centimeters)								
11-20			1					1
21-30	1		3				1	5
31-40	1		5	3			2	11
41-50	2	3	2	2	1		2	15
51-60	9	1	4	2	2		1	19
61-70	4	2	1			2	3	12
71-80	2	3	2			1	4	13
81-90	4			1	1	1	1	8
91-100	4			1				6
101-110	1	1			1	1		4
111-120						1		2
121-130	1						1	2
131-140	1						1	2
141-150				1				1

\*Includes Haffner operation for exophthalmos and tantalum cranioplasty, 3 cases each; cordotomy; section of superficial pituitary nerve, subtemporal decompression, drainage of subdural hematoma and spinofacial anastomosis, 2 cases each; and section of eighth nerve, 1 case.

neurosurgical procedures, regardless of length, in patients over ten years of age.<sup>2</sup> Although this report is based on a planned study of 101 unselected cases in which Pentothal Sodium was the anesthetic agent, we have employed it in several hundred additional major neurosurgical procedures. No death could be attributed to the anesthetic.

The types of operation are listed in Table 1, as well as the age incidence, the duration of the anesthesia and the dosages of Pentothal Sodium.

Seconal Sodium is given two hours before operation. Forty-five minutes before operation adults receive 0.65 mg of atropine and children a proportionately smaller dose. When the patient is extremely nervous or upset, morphine is given with the atropine.

After the patient has been placed in position and the operative site has been prepared, a suitable vein in the hand or forearm is selected for the intravenous administration of 5 per cent dextrose in saline solution. A three-way stopcock is interposed between the intravenous needle and the dextrose solution. Rubber tubing leads from the stopcock to a 20-cc syringe containing the Pento-

\*Fellow in neurosurgery, Cleveland Clinic.

†Neurosurgeon in-chief, Cleveland Clinic.

thal Sodium For the last few years we have used nothing but a 2.5 per cent solution of this anesthetic agent

After the patient has been anesthetized and draped, the line of the incision is thoroughly infiltrated with 1 per cent novocain solution and the operation is begun. A Geudel airway is usually placed in the patient's mouth for the administration of oxygen if necessary.

## OPERATIVE PROCEDURES AND RESULTS

### *Subtentorial Craniotomy*

In our experience, Pentothal Sodium anesthesia has been superior to all others for craniotomies. Because the induction of anesthesia is brief, the patient is under an anesthetic for a shorter time than would be the case if inhalation anesthesia were used. Moreover, since with this anesthetic agent there is no increased intracranial pressure, bleeding is reduced. If used together with local anesthesia, the Pentothal Sodium anesthesia need not be deep and may be lightened after the scalp flap has been reflected. During closure of the scalp wound, the anesthetic may again be deepened if necessary. When the patient is returned to bed, his head is elevated 45 cm. to lower the venous pressure and reduce postoperative oozing. Postoperative vomiting and retching, which are frequent after inhalation anesthesia, cause severe fluctuation in intracranial pressure and increase the tendency to postoperative bleeding. After Pentothal Sodium anesthesia vomiting is an unusual occurrence.

In suspected brain tumors encephalography is frequently employed as a diagnostic procedure. The encephalogram is made in the operating room, and craniotomy is performed immediately after the roentgenograms have been made. This naturally increases the duration of the anesthesia. In 3 sample cases the relative quantities of 2.5 per cent Pentothal Sodium used for pneumoencephalography and craniotomy were as follows: Case 1, 33 and 65 cc., Case 2, 25 and 90 cc., and Case 3, 35 and 60 cc.

That 2 patients in this series of thirty craniotomies required larger than average quantities was attributed to their excessive use of alcohol and tobacco. This is usually true of this type of patient. There were no untoward reactions to the drug in any of these cases.

### *Suboccipital Craniotomy*

There were 11 suboccipital craniotomies in this series. Pentothal Sodium anesthesia was found to have the same advantages for this type of operation as for supratentorial craniotomies. In addition,

the patient is able to co-operate in securing the proper position for operation. This is of great importance because the patient is placed in the sitting position for this operation. In this series the only complication was respiratory obstruction in an extremely obese patient, which was relieved by changing the position of the head.

### *Other Operations*

Section of the sensory root of the fifth nerve in the middle fossa was done in 21 cases. The patient is not anesthetized until after the skin is prepared and the field draped. As soon as the sensory root is sectioned, the anesthetic is discontinued, denervation making the closure painless. Because many of these patients are aged and are poor surgical risks, a short anesthetic is of distinct advantage. There were no untoward reactions in this group.

Lumbar laminectomy for protruded intervertebral disk was done in 10 cases. Pentothal Sodium anesthesia has the disadvantage in this procedure of allowing little muscular relaxation. Accordingly, during the last nine months the operation has been done under spinal anesthesia, supplemented with Pentothal Sodium if the patient is very apprehensive or if the spinal anesthetic wears off before the operation has been completed. There were no reactions in this group.

Dorsal sympathectomy was performed in 6 cases. All the operations were performed with the patient in the sitting position. There were no reactions to the anesthetic.

Laminectomy was performed in 6 cases, either for cord tumor or for protruding intervertebral cervical disk. The only untoward reaction was labored respiration, which was relieved by changing the patient's position.

A patient who suffered from a traumatic head wound had continuous generalized convulsive seizures until 5 cc. of a 2.5 per cent solution of Pentothal Sodium was given. A patient who was being trephined for subdural hematoma developed hiccup and laryngeal spasm, which lasted for ten minutes. When the anesthesia was gradually deepened, both reactions stopped, and the patient's condition remained good for the rest of the procedure.

## SUMMARY

Intravenous Pentothal Sodium anesthesia has been found to be extremely satisfactory and safe for neurologic surgery.

## REFERENCES

1. Gardner, W. J., Nosik, W. A. and Brubaker, R. E. Pentothal sodium anesthesia in pneumo-encephalography: preliminary report. *Cleveland Clin. Quart.* 7:174-177, 1940.
2. Woodhall, B. Pentothal sodium anesthesia in neurologic surgery. *War Med.* 4:556-564, 1943.

CLINICAL NOTE

AGRANULOCYTOSIS FOLLOWING  
MAPHARSEN THERAPY

A REPORT OF

TWO CASES TREATED WITH PENICILLIN

CAPTAIN JOHN F McMANUS, M C, A U S \*

**A**GRANULOCYTOSIS following Mapharsen therapy for syphilis has been a serious but fortunately rare occurrence. The concurrent use of penicillin in the treatment of this complication and of syphilis has not been previously reported. Hence, the following case reports are of interest.

**CASE 1.** A 21-year-old Negro soldier developed a penile ulcer on May 23, 1944. *Treponema pallidum* was demonstrated in a dark-field examination on May 27. The Kahn reaction was negative on May 30. The past history was negative except for gonorrhea in September, 1943, which had been successfully treated with sulfonamides.

Except for the presence of a penile ulcer in the coronal sulcus, the physical examination on admission was essentially negative. The weight was 145 pounds. The blood pressure was 100/60.

Intensive therapy was begun on May 30 and consisted of the daily intravenous injection of 0.066 gm of Mapharsen and the intramuscular injection of 0.2 gm of bismuth subsalicylate in oil every 3 days. A mild Herxheimer reaction followed the first injection of Mapharsen. Treatment was given for 8 days without other adverse reactions. On the 9th day, the patient manifested a moderately severe Milian reaction, and arsenotherapy was omitted for 5 days. Arsenotherapy was resumed on the 14th day, when 0.030 gm of Mapharsen was given. This was followed by a rise in tem-

On the 22nd day, anorexia was more marked and the patient complained of pain and swelling in the region of the left submaxillary lymph nodes. On physical examination he did not appear to be in distress. There was moderate redness and puffiness of the gums, and slight injection of the pharynx. The left submaxillary lymph nodes were tender and slightly swollen. During that day the patient did not feel especially ill and had to be forced to remain in bed. The temperature fluctuated between 102 and 103°F and the maximal pulse was 96. The white-cell count was 3200 with no granulocytes. Treatment on the 22nd and 23rd days consisted of four daily intramuscular injections of 100 mg of B A L in oil. On the 23rd day, the temperature remained elevated and reached a maximum of 103°F, the pulse rose to 112. By that time, the patient looked acutely ill and complained of weakness and nausea. The other signs and symptoms had progressively increased. The white-cell count was 4600, with 1 per cent nonsegmented neutrophils. On the 24th day, the weakness had increased and prostration was marked. It became increasingly difficult for the patient to open his mouth because of the pain and swelling of the left submaxillary lymph nodes. Examination of the mouth and pharynx was essentially the same as previously noted. Neither ulceration nor necrosis was seen. Treatment on that day consisted of the intravenous injection of 1500 cc of 10 per cent glucose in saline solution, in addition to two injections of 100 mg of B A L in oil. The white-cell count was 3300, with no polymorphonuclear leukocytes. In the evening the prostration had increased and the patient appeared critically ill. The temperature was 103°F, and the pulse 112. Forty thousand units of penicillin was given intramuscularly, and repeated every 3 hours for 7½ days.

On the 25th day, there was a decrease in the pain and swelling of the left submaxillary lymph nodes, and prostration was less evident. The maximum temperature was 102°F. In addition to penicillin, the patient was given two intramuscular injections of 100 mg of B A L in oil and a transfusion of 500 cc of citrated blood. The white-cell count prior to the transfusion was 3900, with 2 per cent segmented neutrophils and 2 per cent eosinophils. On the 26th day, improvement continued and the maximum temperature was 101.6°F. The white-cell count on the following day was 4000, with 3 per cent segmented neutrophils, 13 per cent nonsegmented neutrophils, 2 per cent eosinophils and 32 per cent juvenile forms. The highest temperature reached on the two succeeding days was 99.8°F, and the dramatic

TABLE 1 Hematologic Data for Case 1

DATE	RED-CELL COUNT	HEMO- GLOBIN (TALLQVIST)	WHITE- CELL COUNT	SEGMENTED NEUTRO- PHILS	NONSEG- MENTED NEUTRO- PHILS	LYMPHO- CYTES	MONO- CYTES	EOSINO- PHILS	BARO- PHILS	MYELO- CYTES	JUVENILE CELLS
1944	$\times 10^6$	%	$\times 10^3$	%	%	%	%	%	%	%	%
5-30	4.2	85	9.9	—	—	—	—	—	—	—	—
6-3	—	—	5.2	—	—	—	—	—	—	—	—
6-8	4.4	75	11.5	75	15	10	0	0	0	0	0
6-13	—	—	9.6	71	5	17	3	4	0	0	0
6-15	—	95	—	—	—	—	—	—	—	—	—
6-19	—	—	3.2	2	0	54	75	15	4	0	0
6-20	3.7	75	3.2	0	0	41	55	0	4	0	0
6-21	4.4	60	4.6	0	1	49	50	0	0	0	0
6-22	3.3	75	3.3	0	0	49	49	2	0	0	0
6-23	4.3	70	3.9	2	0	51	45	2	0	0	0
6-24	4.2	90	4.0	3	13	46	4	2	0	0	32
6-26	4.3	90	10.1	23	11	30	12	9	6	6	3
6-27	4.6	90	13.7	58	11	21	2	1	0	5	2
7-5	—	90	6.6	62	6	28	2	2	0	0	0

perature to 104.0°F. On the following day the patient was feeling well, and 0.030 gm of Mapharsen was given without any adverse reaction. For the next 6 days, full doses of Mapharsen were given, — 0.066 gm a day, — without any apparent ill effect. On June 19, the 21st day, the white-cell count was 3200, with 2 per cent neutrophils. That evening the patient complained only of slight anorexia. The temperature rose to 100.6°F and the pulse to 80. Thereafter, no more arsenic or bismuth was given. A quantitative blood Kahn reaction had been positive (10 units) on the 13th day. In 21 days of therapy the patient had received sixteen injections of Mapharsen, totaling 0.984 gm, and seven injections of bismuth subsalicylate, totaling 1.4 gm.

clinical improvement that followed paralleled the improvement in the blood picture.

After the 28th day, the patient was afebrile and asymptomatic except for slight, decreasing weakness. Penicillin therapy was completed on the 32nd day. By the 37th day the penile ulcer had healed, physical examination was essentially negative, and the Kahn reaction was negative. The patient was discharged to duty on the 39th day.

In the treatment of the agranulocytosis the patient had received 1200 mg of B A L in oil, 500 cc of citrated blood and 2,400,000 units of penicillin (Table 1).

**CASE 2.** A 23-year-old soldier developed a penile ulcer on August 4, 1944. *T. pallidum* was demonstrated in a dark-field examination on August 17. The qualitative Kahn reaction was positive on that day, and a quantitative test was positive (80 units) on August 22. The past history in-

\*Assistant in medicine, Boston University School of Medicine and junior visiting physician, Sixth Medical Service, Boston City Hospital (on leave of absence).



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tion of toxic drugs, it is of paramount importance to discontinue immediately the use of the drug. Treatment with repeated blood transfusions and the administration of Pentnucleotide, adenine sulfate, liver extract, leukocyte cream and yellow-bone-marrow extract has not been uniformly successful. Many cases have ended fatally because of overwhelming septicemia, in the absence of circulating leukocytes. There have been some cases in which spontaneous recovery occurred. Thus, the control of septicemia is essential to the successful management of patients with agranulocytosis while awaiting the spontaneous or induced recovery of the hematopoietic function of the bone marrow. The sulfonamides have been successfully used in this respect,<sup>7-10</sup> even when the agranulocytosis has been associated with sulfonamide therapy.<sup>11</sup> Agranulocytosis following sulfonamide therapy has been frequently observed, but sulfadiazine is probably the least likely of the sulfonamides to cause serious toxic reactions. On the other hand, fatal granulocytopenia developing during the administration of sulfadiazine has been reported.<sup>12-14</sup> It has been suggested that penicillin might prove a better preparation for the management of severe infection in patients with agranulocytosis.<sup>15</sup>

Cases of agranulocytosis that developed following the use of sulfathiazole in which penicillin was successfully employed have recently been reported.<sup>16, 17</sup> In 2 cases, agranulocytosis complicating Mapharsen therapy for syphilis has been successfully treated with penicillin, but the amount administered was probably inadequate to eradicate the primary infection.<sup>18</sup>

The patient in Case 1 received a total of 1200 mg of BAL in oil by intramuscular injections during the four days after the onset of agranulocytosis. This substance has a double pharmacologic action, first by converting arsenic within the tissues into a nontoxic compound, and second by increasing the elimination of arsenic in the urine. It has been demonstrated that this substance is not toxic in the dosage given and is of distinct value in the treatment of arsenical dermatitis. There was reason to believe that its administration might be of value in other arsenical reactions; hence it was used in Case 1. There was even greater indication for its use in Case 2, because of the coexisting toxic hepatitis, but it was not employed and recovery did not seem to be retarded as a result. But the first patient had received a total of 0.984 gm of Mapharsen prior to the onset of agranulocytosis, whereas the second had received only 0.520 gm. No definite benefit is claimed for its use, however, since the patient receiving it showed neither clinical nor hematologic evidence of improvement until penicillin was given in addition.

The principal reason for using penicillin in these cases was on account of its demonstrated value in the treatment of syphilis. Moreover, there was less risk than in using sulfadiazine, which is capable of producing agranulocytosis. These patients were therefore given penicillin according to the routine that has since been adopted as the one of choice in all patients with primary or secondary syphilis. Sepsis was promptly controlled in both patients, and Case 1 demonstrated a reversal of serologic reaction from positive to negative at the conclusion of treatment. In Case 2, the titer of the Kahn reaction dropped from 80 to 10 units during treatment. It seems probable that this patient has attained seronegativity without further treatment, but this cannot be definitely stated because follow-up serologic reports are not yet available.

### SUMMARY

Two cases of acute agranulocytosis — one with coexisting toxic hepatitis — attributable to Mapharsen therapy for syphilis are reported. Penicillin was of distinct value, both in promoting recovery by combating sepsis and in the treatment of the underlying syphilis.

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cluded an attack of hepatitis in 1942 following vaccination for yellow fever. The patient was a periodically heavy drinker of alcohol.

Except for the presence of two ulcers on the shaft of the penis and bilaterally enlarged inguinal lymph nodes, physical examination was essentially negative. The weight was 150 pounds. The blood pressure was 120/80.

Intensive therapy was begun on August 18, and consisted of daily intravenous injections of 0.065 gm. of Mapharsen and intramuscular injections of 0.2 gm. of bismuth subsalicylate in oil every 3 days. A mild Herxheimer reaction followed the first injection of Mapharsen. Treatment was given for 8 days without other adverse reactions. On the 9th day, the patient developed a moderately severe Milian reaction, and treatment with arsenic and bismuth was omitted and permanently discontinued. In eight days of intensive therapy the patient had received eight injections of Mapharsen, totaling 0.520 gm., and three injections of bismuth subsalicylate, totaling 0.6 gm.

Six days after the last injection of Mapharsen, the patient complained of anorexia and appeared slightly jaundiced. Urinalysis revealed a trace of bile. A diagnosis of toxic hepatitis due to Mapharsen was made. The appetite decreased as the jaundice grew more intense during the next several days. The liver became tender and palpable 1 fingerbreadth below the right costal margin in the midclavicular line. A low-grade fever continued until September 8, when the patient complained of a chill in addition to a sore throat and gums. The temperature rose to 104.6°F. Physical examination revealed, in addition to jaundice and an enlarged, tender liver, a moderately increased redness and swelling of the gums and pharynx. No areas of ulceration or necrosis were seen. The white-cell count was 3850, with 9 per cent

therapy was completed on September 15, at which time the quantitative blood Kahn reaction was positive (10 units). Clinical jaundice was not detectable after September 23. The penile ulcers had entirely healed and physical examination was essentially negative on October 3, when the patient was transferred to the rehabilitation section. He remained there for 1 week and was discharged to duty feeling entirely well. The patient received 2,400,000 units of penicillin in the management of the agranulocytosis and of the primary syphilis. No B A L or blood transfusions were given (Table 2).

Agranulocytosis has been recognized as a serious but rare complication following standard Mapharsen therapy for syphilis. Fatalities have been reported by a number of observers.<sup>1-4</sup> On the other hand, Stephenson, Chambers and Anderson<sup>5, 6</sup> reported a total of over two hundred and eighty-five thousand injections of Mapharsen with no fatalities due to agranulocytosis. Kasich<sup>7</sup> quotes Nelson's series of 4066 patients who had received over fifteen thousand injections of Mapharsen, in 2 of whom blood dyscrasias occurred. No cases of agranulocytosis were reported in a series of 4871 patients who had received intensive Mapharsen therapy.<sup>8</sup> Studies of the sternal bone marrow in 14 patients during intensive arsenotherapy revealed no significant

TABLE 2 Hematologic and Other Data for Case 2

DATE	RED CELL COUNT	HEMOGLOBIN (TALL-QVIST)	WHITE-CELL COUNT	SEGMENTED NEUTROPHILS	NONSEGMENTED NEUTROPHILS	LYMPHOCYTES	MONOCYTES	EOSINOPHILS	BASOPHILS	MYELOCYTES	JUVENILE CELLS	PLATELETS	ICTERIC INDEX	SERUM BILIRUBIN
1944	$\times 10^6$	%	$\times 10^6$	%	%	%	%	%	%	%	%		units	mg/100cc
8-18	—	—	8.3	63	2	31	4	0	0	0	0	—	—	—
8-22	4.7	100	—	—	—	—	—	—	—	—	—	—	—	—
8-25	5.1	100	6.6	67	0	27	0	6	0	0	0	—	—	—
8-29	4.8	90	6.6	66	11	22	1	0	0	0	0	—	—	—
9-1	—	—	—	—	—	—	—	—	—	—	—	—	45	4.3
9-3	—	—	—	—	—	—	—	—	—	—	—	—	54	6.3
9-8	4.6	95	3.8	9	0	77	9	3	2	0	0	—	32	—
9-9	4.3	85	4.6	7	0	58	32	3	0	0	0	Normal	28	—
9-10	4.0	80	3.7	2	1	66	27	4	0	0	0	—	—	—
9-11	3.8	80	7.4	11	0	72	14	3	0	0	0	—	—	—
9-12	3.9	90	8.8	21	4	46	29	0	0	0	0	—	—	—
9-13	4.0	85	11.0	16	12	22	16	8	0	4	21	—	—	—
9-14	4.5	—	10.4	11	13	32	12	9	0	3	19	—	—	—
9-15	4.5	90	11.2	37	11	24	13	9	0	0	6	—	—	—
9-16	4.3	90	11.4	46	6	29	9	6	0	0	4	—	15	1.4
9-17	4.6	80	12.8	57	4	23	9	5	0	0	2	—	—	—
9-18	4.3	85	10.0	58	2	33	2	5	0	0	0	—	—	—
9-19	—	90	8.0	61	1	28	3	5	2	0	0	—	—	—
9-24	—	—	5.4	55	0	34	4	6	1	0	0	—	—	—
9-25	—	—	—	—	—	—	—	—	—	—	—	—	13	—

segmented neutrophils and 3 per cent eosinophils. Penicillin therapy was immediately begun, and the patient was given 40,000 units intramuscularly every 3 hours for the next 7½ days. On September 9, he appeared better and the maximum temperature was 102.8°F. The white-cell count was 4650, with 7 per cent segmented neutrophils, 3 per cent eosinophils and a normal number of platelets.

On the following day improvement continued and the highest temperature was 100.5°F. The white-cell count was 3750, with 2 per cent segmented neutrophils, 1 per cent nonsegmented neutrophils and 4 per cent eosinophils. On September 11, improvement was still more evident and the temperature reached a maximum of 99.4°F. The white-cell count was 7400, with 11 per cent segmented neutrophils and 3 per cent eosinophils. The patient was afebrile on September 12 and remained so thereafter. He had no complaints after that date, and the liver was no longer palpable. The jaundice was still evident, although decreased in intensity. The white-cell count on September 12 was 8800, with 20 per cent segmented neutrophils and 4 per cent nonsegmented neutrophils.

The remainder of the convalescence was uneventful, and the blood picture rapidly returned to normal. Penicillin

effect on either the erythrocytic or the leukocytic series of cells.<sup>9</sup> Kasich<sup>7</sup> has reported 2 cases in which agranulocytosis followed standard Mapharsen therapy. The patients recovered following the use of sulfadiazine, but he does not mention any further therapy for syphilis. Kasich recommends frequent white-cell counts for all patients receiving Mapharsen. When intensive arsenotherapy was made the treatment of choice in this theater for patients with primary and secondary syphilis, the routine of making white-cell counts and differential counts at five-day intervals was adopted. Patients in this hospital received a diet low in fats but high in proteins and carbohydrates. No supplementary vitamins or drugs were used.

To promote recovery in patients who have developed agranulocytosis following the administra-

of scientific medical knowledge organized to the purpose of making this knowledge and skill available to those patients who seek its beneficence

The history of medicine is swift of change. Medical knowledge in its scientific aspects has expanded prodigiously through scientific research, to such an extent that those responsible for the curriculum have an impossible task of holding the essentials for medical education in its fullest sense within the nonelastic limits of time allotment. Choices must be made. At the moment it is the science of medicine that has won out. There is danger that medicine will be thought of as synonymous with the scientific aspects of medicine alone, and not be left free to its broader definition, with scientific medicine held in its true relation to the whole subject. Heroic efforts are being made by many of your clinical leaders to combat the crowding out of these social and humanitarian aspects of medicine. Dr Ryle in his definition of social medicine ably analyzes the situation in medicine today. He contends that as clinical medicine resorts more and more to technical procedures there is less and less intimate understanding of the patient as a person. "Science without humanism," he writes, "may work with atoms but it will not work with men." He argues for recognition of the "interdependence of clinical, social and environmental study" of the patient for "the contribution which each can make to a better appreciation of etiology and prognosis and to a better organization" of medical care. He maintains

Social medicine means what it says. It embodies the idea of medicine applied to the service of man as *socius*, as fellow or comrade, with a view to a better understanding and more durable assistance of all his main and contributory troubles which are inimical to active health and not merely to removing or alleviating a present pathology. It embodies also the idea of medicine applied in the service of *societas*, or the community of men, with a view to lowering the incidence of all preventable disease and raising the general level of human fitness.

One of the correctives that has been resorted to in the Boston hospitals is the inclusion in the medical team of the medical social worker, who is charged with responsibility to bring to the clinician's attention information about the patient as a person in his social setting. Her purpose is to bring into clearer focus the meaning of illness to the patient — its effect on his usual way of life, his responsibilities and unfulfilled family obligations. It is out of such experience as a medical social worker that I speak to you today.

It is *not* the function of the medical social worker to take over all the social responsibility for care of the patient. The patient is the responsibility of the physician. The more aware the latter is of the significance of social factors in the patient's life as they may bear on his illness, the more readily will he make suitable use of the assistance of the social worker. He turns to her to elaborate the brief — too brief — social study of the patient and

to assist him and the patient in working out a practical plan supportive of his medical-care plan.

What are some of the methods of securing pertinent social information? One principle we must accept is that of *individualizing* the patient. For the patient this is entirely acceptable. The patient feels unique — he *is* unique. We can lose ourselves in the group in some situations, — ball games or symphony concerts, — but in illness we are unique. The feeling of the patient about his illness — its meaning to him — is then of first importance.

The trained medical social worker disciplined by working closely with expert clinicians has special reason to appreciate some scientific procedures and principles. She is trained to case study in the area of the social life. She keeps in mind the common need for a normal, satisfactory way of life — namely, satisfying family relations, health, economic independence with good occupational adjustments, freedom in recreational activities and a reasonable degree of fulfillment of one's wishes and interests. The patient's so-called "social situation" prior to illness and as effected by illness is of concern to the medical social worker. She must determine what aspects of this situation may be significant to the physician. The gathering of such data from the patient, his family and others, the correlation of them to the clinical findings in conference with the physician, and planning with the patient and the physician to make available to the patient her experience and resourcefulness are her suitable functions.

I think of the Greek chef who was sent into the hospital ward for study of gastric ulcer. After a few days there, he insisted in broken English that he must go home. A period of three or four weeks of carefully regulated regimen under observation on the ward was advised. The reasons for his resistance to the medical plan were brought to light when his Greek physician and a Greek priest were brought into consultation with the physician in the wards. There was the patient's fear of operation, but chiefly there was his anxiety about the welfare of his wife and three children. After the ward physician's careful explanation of the reason for the hospital stay had been interpreted to him and his wife, and he had received reassurance that his job in a Greek restaurant would be held for him, he calmly accepted the medical plan.

History-taking in medical experience as practiced in our busy wards is almost entirely concerned with the restricted medical situation. The social history is meager and often inadequate. The patient, a highly valuable source of information, may not give the full story. I will give you a case in point that illustrates the nature of social evidence.

A girl of sixteen with ulcerative colitis was admitted to the ward for study and treatment. The original social data on the medical record under "Family History" stated that the mother had died

## SYMPOSIUM ON MEDICAL SOCIOLOGY

## SOME CLINICAL ASPECTS OF SOCIAL MEDICINE\*

IDA M. CANNON†

BOSTON

THE English language sometimes seems to obstruct the processes of thinking. Words may become impoverished, or they may become so weighted with a variety of meanings that when they reach the auditory equipment of a dozen persons they carry twelve different meanings and so cloud mutual understanding. "Social" is one of those words. It would have been helpful to me in tackling the subject of social medicine if I could have known beforehand what the term "social" as related to medicine means to each of you. One has only to refer to the dictionary to find the reason for some of the confusion in its use, for there are given therein at least eleven varieties and shades of meaning. One synonym is given as "convivial." You may judge whether that is pertinent to our discussion today.

For our purpose we might as well leave it that the term "social" is not definitive. Let us accept it as having to do with human interrelations, and pass on to my contention that the phrase "social medicine" is in a sense ambiguous. We may presume to use the phrase "scientific medicine" if we wish to specify one focus of attention within the broad term "medicine." But what about "social medicine," a common phrase these days, and now dignified by a highly significant development at Oxford in the establishment of a professorship of social medicine? In the *British Medical Journal* for November 20, 1943, Dr. John A. Ryle, who holds that chair, has given an excellent statement of his use of the term in his article, "Social Medicine: Its meaning and scope." I have reason to be deeply interested in his presentation, and I can accept the utility of the phrase at this stage in a rethinking of our concept of medicine.

But before I deal with my assignment of addressing you on the subject of social medicine, I wish to register my reasons for objection to the term as ambiguous. Let us accept the brief dictionary definition of medicine in its broad inclusive meaning as "the science and art of dealing with the prevention, cure and alleviation of disease to man." How, then, can medicine as such be other than social? How can it be divorced from its social, its human and community, significances and still be so defined? Even the research laboratory worker, with his attention focused on the study of the blood,

serves the goal of relief of human ills. We may ask how an education in medicine can be justified if it fails to keep clear the ultimate humanitarian purposes of that education.

My desk at the hospital is so placed that I can readily see the ambulance rushing up to the Emergency Ward at any time of the day. It is a rule of the parking space that there must be no obstacle to the approach to the Emergency Ward entrance, where at any moment, day or night, medical care is immediately available for the patient in emergency need, no matter who he is. There is no moralistic question whether he is "worthy" of medical skill, no question of his economic status. He is a patient. That is enough. Other less important questions may have to be considered later, but the immediate urgent medical need is the clear focus of attention. And why do we so easily take this for granted and assume that there is nothing unique in it? Why all this meticulous care? It is characteristic of thousands of hospitals all over the land, and it is a high tribute to the medical profession that this is so.

Obvious and accepted facilities such as these are so characteristic of our social life that we accept them without due appreciation of their significance. There must be meaning in this devoted attention of doctors and nurses to saving human life. What is the reason? Surely not the mere preservation of biologic existence. How tragic it is when the highest medical and nursing skill leaves the patient nothing but breathing and heartbeat, with little capacity to play his part in his social relations. The essential purposes of physicians, surely the "flower of our civilization," as Stevenson termed them, rest in something more than the saving of life itself. Is it not a tacit recognition of the meaning of life? And the deepest meaning of life for us human beings is in our personal, social relations. Its meaning would be bare if we were stripped of our immediate family and those dearest to us, or if our work and play had no comradeship in friendships made more deeply significant through mutual experiences.

It is in terms of disturbances in these relations that patients bring to the hospital with their diseases that I wish to consider the practice of medicine as you are to see it in your hospital experience. The focus will be on the effects of illness on personal and community life and the more distinctly social aspects of medicine. This focus should not blind us to the broad significance of the hospital as bringing to bear on the patients' problems all the wealth

\*This is the first of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March, 1945. They were sponsored by the Department of Preventive Medicine and were primarily intended for third year students. These articles will temporarily replace the reports "Medical Progress."

†Formerly chief of Social Service, Massachusetts General Hospital.

pathology, with due consideration given to minutiae, is time-consuming and tends to limit the area of attention, to the exclusion of a breadth of view. In the light of the vast realm of medicine, we must accept the necessity for specialization, with its deepening and enriching of knowledge and of skills for merciful purposes. Specialization in the social aspects of medicine has come as a logical development of clinical specialization and the necessary organization of services to large numbers of patients in the present-day institutional practice of medicine. Medical practice deprived of specialized knowledge and skills is superficial indeed. How are the high value of specialization and the delegation of responsibility to be applied to adequate care of the patient? Only, I believe, through mutual respect for specialized knowledge and skills and a clear purpose to strive for unity in diversity.

We are a long way from effective integration in the medical care of our patients. The modern scientifically oriented teaching hospital, for instance, presents a complicated array of specialties within clinical medicine, together with several professional groups to whom special services are delegated. When the purpose of care of the patient is the com-

mon bond within this group, there is an opportunity for a high level of democratic functioning. The physician, the nurse, the medical social worker, the dietitian, the occupational and physical therapists, the librarian and the clergyman must each understand the function of the others and recognize without professional jealousies that there are areas of mutual responsibility. I firmly believe that the physician, who must be the leader of the group, should carry the primary responsibility in as broad a scope as his capacity and time allow, and that he should be the one to co-ordinate the special services that complement and supplement his own care of the patient. Such integration of special skills is not as yet the usual practice in modern hospitals.

The humanities as related to scientific medicine call for intelligent study, as one notes the trends of hospitals toward assumption of broader community-health services. In this trend there is sore need for the leadership of well educated medical men, men to whom education has yielded its most precious gift, open-mindedness and flexibility of thought, with a sensitive awareness of social responsibilities.

of possible heart trouble at thirty-two, that the father was living and had recently been discharged from the Army for "malaria", that there were two brothers—one with possible kidney trouble, and that a sister had died of pneumonia at the age of five

Under "Social History," it was recorded that after the death of the mother, the father found it impossible to work and to care for his daughter. The patient was placed in a boarding school, where she said she was quite happy. Following this, she lived with a foster family for five months and was quite dissatisfied, since these people were allegedly unkind to her. For the last six months she had lived with another foster family, in which she was contented and happy. At the time of the report she was attending junior high school, where she was in the tenth grade.

Social investigation through agencies that had been concerned with the family for many years—among them the Society for Prevention of Cruelty to Children—revealed the following facts. The mother deserted the family when the patient was ten years of age, the father, a seafaring man of low intelligence and uncertain responsibility, was unable to care for the children and gave them up to an institution for destitute children. The five-year-old sister was legally adopted, a favorite brother was later placed in a foster home and the patient lost track of him. In 1942, she was placed in a private semidisciplinary home for girls because of her behavior, and since 1943 she had been placed in two different foster homes in an attempt to meet her obvious need for a home and family life.

The patient's own first report of her history was readily understood to express her desire to create out of her fancy a satisfactory family background. It could have served no good purpose to confront this extremely sick girl with the social evidence at hand, but this evidence served well the clinician and psychiatrist, who through the data given by the patient and the facts secured by the medical social worker were able to estimate the psychic trauma of childhood for this sensitive girl. Just as the dread evidence of cancer is left with the surgeon to disclose in due time to the patient or her family, so the psychiatrist may guard social facts until, having gained the patient's full confidence, he deems it wise to face those facts with her and to help her in achieving a more realistic attitude toward life.

Social factors may be etiologically significant, especially in psychosomatic medicine. Surely there are causal factors in disease to be found in an unwholesome physical environment and in industrial hazards, as well as in lack of decent recreational facilities for youth while alluring evil influences flourish around them. Possibly the term "ecology" may serve the purpose better. I further suggest that diagnosis in its fullest meaning would be more significant if the pathologic entity were placed in

the setting of the adverse social factors. The question is not only what kind of patient has the disease but what difficulties beset him in his social relations. Surely one could get a fairer estimate of prognosis if these factors were taken into account and the social worker could help plan social treatment with the patient, in close collaboration with the physician in his medical-treatment plan.

The importance of the patient's participation in treatment is becoming increasingly significant. The old days of pills and powders have passed. As scientific knowledge progresses, as specific dietaries are recognized as therapeutic and as chronic diseases such as arthritis call for a carefully regulated regimen of rest or specific exercises, the patient must share enhanced responsibility for successful treatment. Obstacles to treatment, whether in the patient's attitude or in his social situation, must be overcome.

Last winter a forty-two-year-old patient came to one of our hospitals from a nearby state for treatment of hypertension. He was found to be an excellent candidate for the Smithwick operation. His medical record contained these notes under "Social History": "Married and five children, living and well. Lost present job for medical reasons, couldn't keep up. Afraid of dizziness."

The patient was referred to the social worker, with a report that he had refused the proposed plan for medical care when it was explained that it would mean a few months at home with diet regimen for weight loss, followed by operation with a carefully guarded and lengthy convalescence. The patient had had an industrial accident in 1937 that resulted in amputation of his leg, but in spite of this handicap he had returned to his skilled work in an aircraft factory. His job as drill-press operator entailed lifting heavy steel bolts and feeding them into the machine. He remained sitting while the machine was in operation, but was forced to stand repeatedly while it was being supplied with bolts.

The patient's return to this job was obviously out of the question. Fortunately, he was a resident of a state in which the revised Physical Rehabilitation Act was in effective operation. The surgeon's plan was offered in definite form, and the way was cleared for it through social planning with the patient, the physical-restoration supervisor and the Welfare Department under provision for Social Security Aid to Dependent Children. Careful following of a diet regimen made possible the operative procedure, and after suitable convalescence a program for vocational training in office work was begun.

It is easy to accept the principle that the patient's personal and social situation should be taken into account in the treatment of his disease. It is not so simple to put this into practice in medical care in our busy, modern hospitals and clinics. Time limitation is a serious factor. Focus of attention on

DETERMINATION	MATERIAL ANALYZED	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
Cholesterol esters	Serum	0.5 cc	65 per cent of total cholesterol	Bloor and Knudson <i>J Biol Chem</i> 27, 107, 1916
Glucose	Blood	0.1	70-100 mg per 100 cc (fasting)	Folin <i>Lab Manual Biol Chem</i> 5th ed, p 307, Folin <i>New Eng J Med</i> 206 727, 1932
Hemoglobin		0.05	14-16 gm per 100 cc	Evelyn <i>J Biol Chem</i> 115 63, 1936
Iodine protein-bound (thyroid hormone)	Serum	4	4-8 microgm per 100 cc	Talbot, Butler, Saltzman and Rodriguez <i>J Biol Chem</i> 153 479, 1944
Magnesium	Serum	2	1-2 meq per liter	Briggs <i>J Biol Chem</i> 59 255, 1924
Non-protein nitrogen	Serum	0.5	15-35 mg per 100 cc	Folin <i>Lab Manual Biol Chem</i> , 5th ed, p 265
Oxygen Capacity	Blood	3	19-22 vol per cent	Van Slyke and Neill <i>J Biol Chem</i> 61 523, 1924, Peters and Van Slyke <i>Quant Clin Chem</i> , Vol II (Methods), p 321
Arterial content	Blood	3	18-21 vol per cent	<i>Ibid</i>
Arterial percentage saturation	—		94-96 per cent	(Arterial content $\times$ 100) $\div$ capacity
Venous content	Blood	3	10-16 vol per cent	<i>Ibid</i>
Venous percentage saturation	—		60-85 per cent	(Venous content $\times$ 100) $\div$ capacity
pH(reaction)	Serum	0.2	7.35-7.45	Hastings and Sendroy <i>J Biol Chem</i> 61 695, 1924, Peters and Van Slyke <i>Quant Clin Chem</i> Vol II (Methods), p 796
Phosphatase, acid	Serum	1	0.5-2.0 units per 100 cc	Gutman and Gutman <i>J Biol Chem</i> 136 201, 1940
Phosphatase alkaline	Serum	0.5	2.0-4.5 units per 100 cc †	Bodansky <i>J Biol Chem</i> 101 93, 1933 (using the above method for determining inorganic phosphorus)
Phosphorus inorganic	Serum	0.2	3.0-4.5 mg per 100 cc *	Fiske and Subbarow <i>J Biol Chem</i> 66 375, 1925, Folin <i>Lab Manual Biol Chem</i> , 5th ed, p 341 (modified for photocolormeter)
Potassium	Serum	3-4	3.5-5.0 meq per liter	Fiske and Litaczek in Folin <i>Lab Manual Biol Chem</i> , 5th ed, p 353
Protein total	Serum	0.5(macro) 0.05(micro)	6.5-8.0 gm per 100 cc	Macro Peters and Van Slyke <i>Quant Clin Chem</i> , Vol II (Methods), p 691 Micro Lowry and Hastings <i>J Biol Chem</i> 143 257, 1942
Albumin	Serum	0.5	4.5-5.5 gm per 100 cc.	<i>Ibid</i>
Globulin	Serum	0.5	1.5-3.0 gm per 100-cc	<i>Ibid</i>
Prothrombin clotting time	Plasma	0.5	By control	Quick <i>J A M A</i> 110 1658, 1938
Purvic acid	Blood	2	0.7-1.2 mg per 100 cc (fasting)	Friedemann and Haugen <i>J Biol Chem</i> 147 415, 1943, Bueding and Wortis <i>Ibid</i> 133 585, 1940
Sodium	Serum	0.5	136-145 meq per liter	Butler and Tuthill <i>J Biol Chem</i> 93 171, 1931
Urea nitrogen	Serum	1	10-28 mg per 100 cc	Van Slyke <i>J Biol Chem</i> 73 695, 1927, Peters and Van Slyke <i>Quant Clin Chem</i> , Vol II (Methods), p 372
Uric acid	Serum	1	3-5 mg per 100 cc	Folin <i>J Biol Chem</i> 101 111, 1933

\*In the newborn infant values may be as high as 6 mg per 100 cc, which then diminish during the first year, in childhood they approach the normal adult average value of 3.5 mg

†The value parallels the rate of growth, diminishing from approximately 14 units per 100 cc. in infancy to 5 units in adolescence and thereafter being maintained at approximately 3.5 units



## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*BENJAMIN CASTLEMAN, M.D., *Associate Editor*EDITH E. PARRIS, *Assistant Editor*

## NORMAL LABORATORY VALUES

To provide ready reference to the normal laboratory values recorded in the "Case Records of the Massachusetts General Hospital" and to the methods used the following tabular summary has been prepared\* and is substituted for one of the

cases. A limited number of reprints will be available and will be forwarded, so long as the supply lasts, to readers of the *Journal* on request, provided that an addressed and stamped (1½ cents) return envelope (approximately 4 by 9 inches) is enclosed. All requests should be addressed to Miss Edith E. Parris, Massachusetts General Hospital, Boston 14.

\* \* \*

## Blood, Plasma or Serum Values

DETERMINATION	MATERIAL ANALYZED	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
		cc		
Amino acids (CO <sub>2</sub> of carboxyl carbon)	Plasma	2	3-5 mg per 100 cc	Hamilton and Van Slyke <i>J Biol Chem</i> 150:231, 1943
Amylase	Serum	2	15-35 units per 100 cc	Adapted from Somogyi <i>J Biol Chem</i> 125:399, 1938
Ascorbic acid (vitamin C)	Plasma	0.5	0.4-1.0 mg per 100 cc (fasting)	Butler, Cushman and MacLachlan <i>J Biol Chem</i> 150:453, 1943
Ascorbic acid	White cells	8 (whole blood)	25-40 mg per 100 cc	<i>Ibid</i>
Bilirubin (van den Bergh test)	Serum	2	Direct, 0.4 mg per 100 cc, indirect (total) 0.7 mg per 100 cc	Malloy and Evelyn <i>J Biol Chem</i> 119:481, 1937
Calcium	Serum	2	9.0-10.5 mg per 100 cc †	Fiske and Logan <i>J Biol Chem</i> 93:211, 1931, Folin <i>Lab Manual Biol Chem</i> 5th ed., p. 351
Carbon dioxide (content)	Serum	0.5	26-28 meq per liter ‡	Van Slyke and Neill <i>J Biol Chem</i> 61:523, 1924, Peters and Van Slyke <i>Quant Clin Chem</i> , Vol. II (Methods), p. 283
Carotenoids total	Serum	2	100-300 int units per 100 cc	Josephs <i>Bull Johns Hopkins Hosp</i> 65:112, 1939 (modified for photocolormeter and calibrated with haliver oil of specified vitamin A content)
Vitamin A	Serum	2	40-100 int units per 100 cc	
Chloride	Serum	0.5	100-106 meq per liter	Wilson and Ball <i>J Biol Chem</i> 79:221, 1928
Cholesterol	Serum	0.5	150-230 mg per 100 cc	Bloor <i>J Biol Chem</i> 24:227, 1916

\*The chemical data were prepared by G. Margaret Rourke, chief of the Chemical Laboratory, Elaine A. MacLachlan, consultant, and Allan M. Butler, staff physician in charge of the Chemical Laboratory.

†Since the total serum calcium concentration is dependent on the serum protein concentration, evaluation of the significance of a serum calcium value requires a serum protein determination.

‡Values in infants and children may be from 20-26 meq per liter. Milliequivalents per liter equal volumes per cent divided by 2.2. The milliequivalent total CO<sub>2</sub> minus 1.3 is usually about equal to the HCO<sub>3</sub> expressed as milliequivalents per liter. For reason for using milliequivalents as units of concentration here and for other electrolytes see Butler and Talbot *New Eng J Med* 231:20, 1944.

DETERMINATION	AMOUNT ADMINISTERED	MATERIAL ANALYZED	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
			cc		
Galactose tolerance	0.5 gm per kg intravenously	Blood	1	Less than 5 mg at 75 min	Basset, Althausen and Coltrin <i>Am J Digest Dis &amp; Nutrition</i> 8:432, 1941
Hippuric acid	1.77 gm sodium benzoate intravenously	Urine	1-hr sample	Greater than 1 gm	Quick, Ottenstein and Weltchek <i>Proc Soc Exper Biol &amp; Med</i> 38:77, 1938, Moser, Rosenak and Hasterlik <i>Am J Digest Dis &amp; Nutrition</i> 9:183, 1942

\*The 2-mg method is used in patients with slight jaundice, and the 5-mg method in patients without jaundice, the method is valueless in patients with obvious jaundice

### Renal-Function Tests

DETERMINATION	AMOUNT ADMINISTERED	MATERIAL ANALYZED	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
			cc		
Phenolsulfon-phthalein	1 cc intravenously	Urine	Total output	25 per cent or more in first 15 min, 40 per cent or more in 30 min, 55 per cent or more in 2 hr	Chapman <i>New Eng J Med</i> 214:16, 1936
Urea clearance	0	Blood and urine	Blood, 1 cc, urine, two 1-hr samples	75 to 125 per cent of normal	Peters and Van Slyke <i>Quant Clin Chem</i> , Vol II (Methods), p 564

### Hematologic Values

DETERMINATION	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
	cc		
Bleeding time	—	Below 4½ min	Lee and White in Todd and Sanford <i>Clin Diag by Lab Methods</i> , 10th ed, p 199
Clotting time	10	Below 20 min	Duke <i>J A M A</i> 55:1185, 1910
Sedimentation rate (two methods)	4	Less than 0.35 mm per min	Rourke and Ernestine <i>J Clin Investigation</i> 8:545, 1930
	4	Less than 15 mm per hr	Modification* of Wintrobe and Landsberg <i>Am J M Sc</i> 189:102, 1935
Hematocrit (percentage volume of packed red cells)	2	Male, 40–54 per cent, female, 37–47 per cent	<i>Ibid</i>
Hemoglobin	0.05	14–16 gm per 100 cc	Evelyn <i>J Biol Chem</i> 115:63, 1936
Mean corpuscular volume	—	80–94 cu microns	(Hematocrit $\times 10$ )—red cells (in millions)
Mean corpuscular hemoglobin	—	27–32 micromicrogm	(Gm of hemoglobin $\times 10$ )—red cells (in millions)
Mean corpuscular hemoglobin concentration	—	33–38 per cent	(Gm of hemoglobin $\times 100$ )—hematocrit

\*Internal diameter of tube should be 4 mm instead of 2.5 mm

## Urine Values

DETERMINATION	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
	cc		
Albumin (quantitative)	10	0-	Folin <i>Lab Manual Biol Chem</i> , 5th ed, p 225
Creatine	24-hr sample	Less than 100 mg per 24 hr *	Folin <i>Lab Manual Biol Chem</i> , 5th ed, p 163
Creatinine	24-hr sample	15-25 mg per kg †	<i>Ibid</i> , p 159 (modified for photocolormeter)
Diastase	2	Dilution of 1 4 to 1 16	Stitt <i>Pract Bact Haem &amp; Parasitol</i> , 9th ed, p 731
Follicle stimulating hormone	24-hr sample	Before puberty, less than 65 mouse units per 24 hr, after puberty 65-52 mouse units per 24 hr, after menopause 104-600 mouse units per 24 hr	Klinefelter, Albright and Griswold <i>J Clin Endocrinol</i> 3 529, 1943
Sugar			
Total (quantitative)	5	0	Benedict <i>J A M A</i> 57 1193, 1911
Total (roughly quantitative)	0.5	0	Somogyi <i>J Lab Clin Med</i> 26 1220, 1941
Fermentable	1	0	Hawk and Bergheim <i>Pract Physiol Chem</i> , 10th ed, p 750
Fructose	1	0	<i>Ibid</i> , p 772
Galactose or lactose	6	0	(Total sugar x 1 24) minus fermentable sugar
Osazone, differentiation of	5	0	<i>Ibid</i> , p 50
Urobilinogen	10	Dilution of 1 4 to 1 30	Wallace and Diamond <i>Arch Int. Med</i> 35 698, 1925
17-ketosteroids	12-hr sample	Under 8 yr, 0-2 mg per 24 hr, adolescents, 2-20 mg per 24 hr, males, 8-20 mg per 24 hr, females, 5-14 mg per 24 hr	Talbot, Butler, MacLachlan and Jones <i>J Biol Chem</i> 136 365, 1940, Fraser, Forbes, Albright, Sulkowitch and Reifenschein <i>J Clin Endocrinol</i> 1 234, 1941

\*Per kilogram of body weight, the excretion is higher in women and children than in men, and still higher in infants

†The value depends on the ratio of muscle to fat in the body mass of the patient. The higher the ratio the greater the creatinine excretion per kilogram of total body weight. Because this ratio is low in infants, the excretion per kilogram is low.

## Liver-Function Tests

DETERMINATION	AMOUNT ADMINISTERED	MATERIAL ANALYZED	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
			cc		
Bromsulfalein*	2 mg per kg intravenously	Serum (30 min after injection)	2	Less than 5 per cent retention	Rosenthal and White <i>J A M A</i> 84 1112, 1925, Peters and Van Slyke <i>Quant Clin Chem</i> , Vol II (Methods), p 910
	5 mg per kg intravenously	Serum (45 min after injection)	2	Less than 5 per cent retention	<i>Ibid</i> (modified, i.e., result $\div 2.5$ )
Cephalin flocculation	0	Serum	0.2	Up to ++ in 48 hr	Hanger <i>J Clin Investigation</i> 18, 261, 1939

beneath the left fourth, fifth, and sixth ribs anteriorly. This portion of the lung fields, which was near the lateral chest wall, was somewhat obscured by the closely grouped overlying ribs. The remainder of the lung fields did not appear remarkable. The heart was not enlarged but was rounded in the region of the left ventricle. The aorta was tortuous. Another film taken two days later again showed a somewhat triangular-shaped area of increased density against the posterolateral chest wall on the left. A linear area of increased density was present in the left costophrenic angle posterolaterally. There was a hazy area of increased density just to the right of the heart, apparently in the middle lobe.

Soon after admission the patient became markedly orthopneic. After vomiting bloody, bile-tinged fluid, he expired on the fourth hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR FRANCIS D MOORE This is the story of a man who had had a gall-bladder operation many years before entry and subsequently had a train of events that might or might not have been related to the cholecystectomy. He finally died of what appears, at least on the surface, to have been a third disease.

The history is of the greatest importance in trying to decide the cause of his jaundice. There are a few things not mentioned in the record that would have been a great help in that regard. We read that during the years after the cholecystectomy he had had several attacks of jaundice, each lasting a few days. We should like to know whether there was pain with the jaundice. If a patient has had a cholecystectomy and then postoperatively has bouts of pain and jaundice that pass off spontaneously, one is justified in thinking that a few common-duct stones were left in the duct, which he is passing off one after another, or possibly that he is suffering from that mysterious entity known as "biliary dyskinesia." If the attacks were painless, they were possibly attacks of cholangitis, in which case one would expect fever and possibly chills.

We should also like to know whether there was a long free interval between these postoperative attacks and the train of events that later led up to his last admission. In other words, was there a period of several years when he was free from pain and jaundice? This is important as it would make one feel reasonably confident that retained common-duct stones were not a factor in his fatal illness.

DR RONALD C SIFFEN I might say in partial answer that Dr E P Hayden saw the patient about four months before the jaundice developed. At that time the patient complained of vague abdominal symptoms. A complete gastrointestinal series was done, but nothing was found.

DR MOORE That tends to make persistent common-duct stones following cholecystectomy less likely.

In his final illness he had a rapid crescendo of pain and jaundice and had itching, a common symptom in extrahepatic biliary obstruction. From that point on, the record tells us of the physical findings and laboratory data in a man with non-inflammatory extrahepatic biliary obstruction, which was incomplete.

My reasons for making these statements are that he had a normal white-cell count and temperature, and it is therefore reasonable to assume that he did not have a primary inflammatory process. The obstruction seems to have been extrahepatic rather than parenchymatous partly because of the high ratio of the direct to the indirect bilirubin, almost 90 per cent, which is quite characteristic of extrahepatic biliary obstruction, and also because with this high total bilirubin there was little evidence of liver-cell damage. The prothrombin time was slightly elevated, it is true, but the albumin-globulin ratio was normal. In other words, the degree of obstruction seems to have been out of proportion to the liver damage.

I do not believe that the obstruction was complete because the patient had bile in his stools, they were brown and showed a chemical test for bile, and just before he died he vomited bile-stained material, which also tells us that the pylorus was patent. We can therefore say that he had incomplete non-inflammatory extrahepatic biliary obstruction and, in addition, bleeding into the gastrointestinal tract, since he passed guaiac-positive stools and vomited some blood just before he died. Incomplete extrahepatic obstruction and bleeding into the gastrointestinal tract should be absolutely diagnostic of carcinoma at the ampulla of Vater, but before we discuss what is wrong with that diagnosis, we might see the x-ray films of the chest.

DR CLAYTON H HALE The films taken at the first examination demonstrate a somewhat triangular shadow of increased density at the level of the anterior portions of the fourth, fifth and sixth ribs. In the lateral projection, this area of increased density is seen to lie posteriorly and there is a slight suggestion of rarefaction in the central portion of the mass. There is also evidence of a healed infarct in the left costophrenic sinus. The cardiac and vascular shadows and the remainder of the lung fields are not remarkable. No significant change is demonstrated on the films taken two days later. From the x-ray finding one must give first consideration to multiple infarcts but the possibility that the large area of density is due to metastatic cancer must be given serious thought.

DR MOORE How often do you see areas of diminished density in uninfected pulmonary infarcts?

DR HALE They are unusual. The possibility of this being a septic infarct must be considered if there is actual rarefaction in the area. The possibility of an abscess, although it is not at all typical,

## Spinal-Fluid Values

DETERMINATION	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
	cc		
Initial pressure	—	70–180]mm of water	
Cell count	0.2	0–5 mononuclear cells (lymphocytes)	
Chloride	2	120–130 meq per liter	Same as that for serum (see above)
Protein	0.6	15–45 mg per 100 cc	Ayer, Dailey and Fremont-Smith <i>Arch Neurol &amp; Psychiat</i> 26 1038, 1931
Glucose	1	50–75 mg per 100 cc	Same as that for blood (see above)
Colloidal gold	0.1	0000000000	Wuth and Faupel <i>Bull Johns Hopkins Hosp</i> 40 297, 1927

## Miscellaneous Values

DETERMINATION	MATERIAL ANALYZED	MINIMUM QUANTITY REQUIRED	NORMAL VALUE	METHOD
		cc		
Stool fat		Representative sample	Less than 30 per cent dry wt	Tidwell and Holt <i>J Biol Chem</i> 112 605, 1936
Calculi		Representative sample		McIntosh and Salter <i>J Clin Investigation</i> 21 751, 1942
Congo red test	Serum	2	More than 60 per cent retention in serum after 1 hr	Bennhold <i>Deutsches Arch f klin Med</i> 142 32, 1923

## CASE 32011

## PRESENTATION OF CASE

A seventy-four-year-old man entered the hospital complaining of jaundice.

Ten years before admission the patient underwent a cholecystectomy. Gallstones were found. During the years after the operation he had several attacks of jaundice, each lasting a few days. Seven months before admission he began to have increasingly severe attacks of epigastric pain, radiating to the chest and to the right costovertebral angle. He also noticed nausea and frequent gaseous eructations. He had lost considerable weight. Ten days before admission jaundice and itching appeared and rapidly increased in severity.

On physical examination the patient was emaciated, weak and deeply jaundiced. The heart was slightly enlarged to the left. A systolic murmur and a diastolic murmur were heard at the apex. The right chest was more prominent than the left, which showed lateral flattening. Rales were heard at both bases. The abdomen was flat and soft. The

liver was tender and enlarged, extending four finger-breadths below the costal margin. An upper-right-rectus scar and a herniorrhaphy scar were present. The reflexes were normal.

The temperature was 98°F, the pulse 75, and the respirations 20. The blood pressure was 150 systolic, 85 diastolic.

The urine was normal except for a ++++ test for bile. The red-cell count was 3,820,000, with a hemoglobin of 12.8 gm. The white-cell count was 7200. The serum bilirubin was 28.5 mg per 100 cc, direct, and 30.3 mg indirect. The prothrombin time was 24 seconds (normal, 18 seconds). The bleeding time was 2½ minutes, and the clotting time 4 minutes. Clot retraction was normal. The total serum protein was 6.5 gm per 100 cc, with 4.3 gm of albumin and 2.2 gm of globulin. The nonprotein nitrogen was 19 mg per 100 cc, and the chloride 95 milliequiv per liter. A stool specimen was light brown and guaiac positive, it was slightly positive for bile.

An x-ray film of the chest taken on the first hospital day showed an area of hazy increased density

fibrous tissue. There were metastases to the regional lymph nodes and the wall of the common bile duct contained a 3-mm nodule of metastatic tumor, which had not eroded the mucosa. I wonder if this small nodule could have caused the pain.

The lungs showed a bilateral bronchopneumonia concentrated in the lower lobes. The density mentioned in the x-ray report was due, I imagine, to a 4-cm area of metastatic cancer in the left lower lobe.

DR MOORE: Perhaps his death was not so sudden as the record indicates. Was the cause of death bronchopneumonia?

DR SNIFFEN: I do not know why he died suddenly.

As incidental findings, the prostate was hyperplastic, with a large median bar, and one section contained a minute focus of primary carcinoma. The large median lobe had led to hypertrophy of the bladder, cystitis, a left hydroureter and ureteritis, and left acute and chronic pyelonephritis.

DR MOORE: You found no cause for the bleeding?

DR SNIFFEN: No, the duodenal mucosa was intact.

cannot be ruled out. A malignant neoplasm, either primary or metastatic, must also be kept in mind.

DR. MOORE: How often do you see areas of diminished density in metastatic cancer?

DR. HALE: We do not see them often.

DR. MOORE: The x-ray films are confusing. From the written record I thought that the x-ray description was characteristic of pulmonary infarction, and the clinical course suggests two or three warning attacks, with a subsequent massive infarct and death. The area that Dr. Hale says is suggestive of septic infarct and abscess is disturbing. It is difficult to believe that there was pulmonary supuration in a man who had a normal temperature and white-cell count. I shall have to reserve judgment on the pulmonary lesion and say that it was probably due to metastatic cancer.

What was the fundamental disease in the abdomen? I have said that many of the characteristic findings were those of carcinoma in the region of the ampulla of Vater, but there are some things wrong with that diagnosis. In the first place, the patient had quite a lot of pain. Carcinoma in the lower portion of the common duct and head of the pancreas is usually accompanied by painless jaundice. There is one explanation, however, for pain in this man. With obstruction to the common duct, the gall bladder is ordinarily greatly distended, and part of the clinical picture of carcinoma of the head of the pancreas is a big gall bladder, which serves partly to decompress the biliary tree. This man did not have a gall bladder to distend. Possibly this absence of a gall bladder accounts for the pain. It is also interesting that we have seen several patients in the last two years who had had previous gallstones and in whom the gall bladder had been removed, and who several years later developed carcinoma lower down in the biliary tree. It makes one wonder if cholelithiasis is part of the background of biliary-tract carcinoma in general, as well as of cholecystic carcinoma itself.

How about common-duct stone? I have already mentioned that it would be unusual for him to have had a long period free of pain if he had had a common-duct stone. It is rare for a person to walk around with common-duct stones for ten years, because they are intermittently extremely painful and should have caused trouble much sooner. If we knew that the gall bladder contained large gallstones and that the cystic duct was normal at the first operation, I should be willing to rule it out completely.

How about other tumors? A tumor higher in the biliary tree, away from the ampulla of Vater, can bleed down the duct and into the gastrointestinal tract, but that is very rare. Carcinoma of the duodenum is a possibility, but it, too, is extremely rare. What about carcinoma of the pancreas? He certainly could have had a carcinoma of the pancreas

that obstructed the duct, but because of the bleeding, I think that this was a lesion directly continuous with the lumen of the gastrointestinal tract. I have already discussed intrahepatic jaundice. Possibly his bleeding was from varices. How about carcinoma of some other organ? Dr. Linton\* has described several cases of carcinoma of the colon and duodenum in which continuity between the duodenum and the transverse colon had been established, with a duodenocolic fistula and jaundice. There was no barium enema on this man, such a diagnosis, however, is only a remote possibility.

As I have said before, I think that he had pulmonary infarcts, but it is too bad that we have no mention of what the lungs showed on physical examination. It might help us to decide on the pulmonary lesion.

My diagnosis, therefore, is carcinoma in the region of the ampulla of Vater. I rule out a common-duct stone. I believe that the cause of death was a massive pulmonary infarct and that the previous pulmonary lesion was an infarct. But the latter, as Dr. Hale has pointed out, might have been a metastatic lesion or some form of abscess.

#### CLINICAL DIAGNOSIS

Carcinoma of pancreas

#### DR. MOORE'S DIAGNOSES

Carcinoma at the ampulla of Vater, with direct invasion of the duodenum  
Pulmonary infarction?  
Pulmonary metastases?

#### ANATOMICAL DIAGNOSES

**Papillary adenocarcinoma of head of pancreas, with metastases to common bile duct and lung**  
Early obstructive cirrhosis of liver  
Jaundice  
Bronchopneumonia

#### PATHOLOGICAL DISCUSSION

DR. SNIFFEN: At autopsy the patient was deeply jaundiced. The liver was dark green and enlarged, weighing 2050 gm. The sections microscopically suggested an early obstructive cirrhosis. The common bile duct was dilated down to the ampulla, which admitted a fine probe. The head of the pancreas seemed a little larger than normal, but the body and tail were atrophic and fibrous. Sections taken through the head of the organ showed microscopically a papillary adenocarcinoma, whereas the parenchyma of the body and tail had undergone atrophy, leaving the islets embedded in dense

\*Linton, R. R. Two stage operation for carcinoma of transverse colon producing duodenocolic fistula: report of two cases. *Arch Surg* 48: 197-207, 1944.

giving increasing attention to a variety of programs designed to change existing arrangements between physicians and society. In times of rapid change it is even more than usually incumbent on physicians to know themselves, for theirs is the responsibility to direct the change in so far as it involves medical affairs. Physicians must continue to be educated, equipped, supported and stimulated to do a good job. To act intelligently they must know what kind of physicians America should have and in what kind of society these physicians are to work.

In these days when technical advance holds the center of the stage, most medical students have little opportunity to learn about either the relations between physicians and society or those between economics and disease. Few are able to approach the social or economic problems of the profession with the same intelligent attitude with which they face illness. Their education has been excellent from the technical point of view, but many of the fundamental problems besetting the profession of which they are about to become members have not been mentioned. Only a few students have interested themselves in these matters outside their studies.

Considerable impetus has been given to the teaching of such subjects by the Interim Report of the Social and Preventive Medicine Committee of the Royal College of Physicians of London.<sup>1</sup> Additional impetus has come from the establishment of a professorship of social medicine in Oxford University. An excellent definitive report has come from the latter source.<sup>2</sup>

As an experiment in teaching, in the winter of 1945 a series of nine lectures for third-year students was given under the auspices of the Department of Preventive Medicine of the Harvard Medical School, much of the stimulus having come from the

students themselves. The first of these lectures was devoted to the broad problem of the individual as a social being and to the effect of social and environmental factors on his health. The material in this lecture is considerably augmented by work on individual patients in the final medical-school year. The remaining eight lectures were given as a series on medical sociology. The lectures were concerned with the study of physicians and the

medical profession in relation to society. Forces determining the past, present and future structure of medical practice were considered. The obligations and responsibilities of the medical profession to society were brought clearly into focus. The speakers at all but the last three lectures were requested to present factual material and not their personal opinions or interpretations. It was thought

that after having heard the factual data, the student would be in a position to reach his own conclusions, and to agree or disagree with the various opinions and points of view expressed in the final lectures. That some of the lecturers committed themselves as advocates of change is both natural in a free society and healthy for the future of medicine. The majority of the students and physicians attending the lectures expressed the opinion that they were helped in objectively facing the problems before them.

In view of the general interest to the medical profession of the problems presented and of the apparent success of this experiment in teaching, these lectures will be printed in consecutive issues of the *Journal*, beginning with this week's issue. It is hoped that they will be provocative of thought and interest on the part of physicians.

#### REFERENCES

1. *Interim Report of the Social and Preventive Medicine Committee of the Royal College of Physicians of London*. 31 pp. London: Harrison & Sons Ltd., 1943.
2. Ryfe, J. A. Social medicine: its meaning and its scope. *Milbank Mem Fund Quart.* 22:58-71, 1944.

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## PEPPER BILL

APPEARING elsewhere in this issue of the *Journal* is an informational report by the Subcommittee on Medical Economics of the Postwar Planning Committee that deserves careful reading by every member of the Massachusetts Medical Society

Last fall this subcommittee was faced with the responsibility of making recommendations concerning the Wagner-Murray-Dingell Bill (S 1050) and the Pepper Bill (S 1318). Since it was wisely decided that such action was impossible in the absence of clearly defined basic principles governing medical-care programs, the subcommittee proceeded to create a set of eight principles that appeared to be essential to any medical-care plan in a free society

Then, on the basis of these principles and of facts more generally regarded as necessary in medical care, the Pepper Bill was carefully studied

As indicated in its report, the subcommittee favors the objectives stated in the introduction to the bill but it also believes, for various reasons, that the bill does not represent the best form of legislation to accomplish what is intended

The report of the subcommittee has been accepted, with minor modification, by the Postwar Planning Committee, the Committee on Legislation and the Committee on Public Relations, and it will be presented to the Council of the Massachusetts Medical Society for acceptance as a joint recommendation

All this represents intelligent action. There is no doubt that the medical profession is threatened with national legislation that, if enacted, would largely abolish medical practice as it is known today. Nothing is accomplished by the mere statement that a plan is "no good." Constructive criticism is required in other words, those who are responsible for administering medical care and hence who are better informed concerning its practical aspects than are those not so engaged must point out *why* a scheme is unwise. In this way it is hoped that the desirable features of such plans can be promoted and that the undesirable ones can be avoided

## MEDICAL SOCIOLOGY

"Know thyself" is a wise command. For physicians, knowledge of themselves implies a judgment whether or not they are doing a good job in an imperfect world. For the individual physician, this judgment is easy to make regarding his technical work, but is difficult to appraise in relation to his equally important social functions. In the latter sphere, the facts are hard to come by, the objectives are poorly defined, and the opinions encountered are often based on emotion

Physicians know that the world is changing at a breath-taking rate, and that the ways by which they serve the people need to be adjusted from time to time, if they are to continue to do a good job. Laymen are also aware of these facts and have been

ored by the Massachusetts Medical Society, as stated in the September 20 issue of the *New England Journal of Medicine*

**Fee-for-service** Under a fee-for-service system, practitioners, specialists and consultants are paid stated value for each unit of service rendered

In current plans the physician is required to submit to the administrative agency a clinical report and a bill or voucher for each service rendered. This entails the administrative costs of handling such reports and vouchers and may require the administrative agency to set up a system of cross index concerning the practices of each physician and the health of each patient

When a doctor cares for few patients under a medical-care plan, fee-for-service provides a remuneration that is proportional to the service rendered and thus covers the uneven incidence of illness among such patients

Under any system of payment, fee-for-service is an appropriate way to pay for consultant or for emergency services not rendered by the patient's family doctor

Under medical-care plans, experience shows that this method of payment is susceptible to abuse by a small percentage of physicians and patients. If the total budget of the medical-care plan is limited and demands are in excess of the funds, the payment per unit of service may be reduced

**Per capita** The per-capita system applies primarily to general practitioners. Under this system, practitioners are paid a certain sum per patient per year for each patient who elects him and whom he accepts. This payment is made regardless of the amount of care given to different patients or the fact that some patients will receive no service. A doctor being paid on this basis may be paid in addition for consultant or unusual services on a fee-for-service or per-case basis

The practitioner is required to notify the administrative agency when he first becomes the practitioner of a given person. This provides the administrative agency with the necessary information for remuneration of physicians. The administrative agency may from time to time request additional information from the doctor for study or other informative purposes. Physicians are usually given the choice of receiving remuneration quarterly, semiannually or annually

When a doctor cares for enough patients under a medical-care program to provide an actuarially sound distribution of risk due to the uneven incidence of illness among his patients, the per-capita method of payment permits economy in administrative burden with equity to the doctor

This method of payment is not susceptible to excessive care by the practitioner but is susceptible to excessive demands by the patient

**Salary** Under the salary method, a stipulated compensation for services rendered is regularly paid a physician, usually per week or per month

For certain physicians practicing as members of well organized groups or institutions, this form of payment provides a graded and predictable remuneration

It may provide the means of attracting a physician to a rural community to which he otherwise would not go because of irregularity of income

If groups of physicians or institutions contract to provide medical care either as consultants, specialists or practitioners, salary may in certain instances be a desirable form of paying for the medical care so provided

If provision is made on a merit basis for advancement and increased salary, the competition for high-salaried positions provides the incentive to a high quality of endeavor on the part of physicians, just as it does in other professions and occupations

This method of payment necessitates but little administrative paper work

**Per case** Under the per-case method a physician is paid a stipulated sum for the total service he renders a patient during a particular illness or because of a particular condition, usually within a stated time

It is particularly applicable to consultant or specialist services rendered to certain types of cases

Under the per-case basis a single clinical report and a bill are usually required to be submitted only at the termination of the services rendered

**Per session** The per-session method applies a flat rate of payment for the services rendered per stipulated session

Payment on this basis is particularly applicable to services rendered intermittently in group clinics

It usually requires the submission of a report of the physician's presence at the session

**Cash indemnity** Under the cash-indemnity system, payments are made by the administrative agency to the patient, not to the doctor. It provides for payment of a flat sum for wages for time lost because of illness or cash payments toward the cost of medical care according to a fee schedule, or both. Each person is free to make his own arrangements with those who furnish medical services as to both the amount of service and the charges for it

It provides no assurance that the money paid to the patient will be expended on medical care, and little control over quality or cost. Such supervision as would check on the expenditure of the funds for the medical care for which they were allotted and on the cost and quality of the care provided would entail an almost insurmountable task

Physicians might be obliged to spend time on examination for certification of illness to permit

## MASSACHUSETTS MEDICAL SOCIETY

### SUBCOMMITTEE ON MEDICAL ECONOMICS, POSTWAR PLANNING COMMITTEE

#### INFORMATION CONCERNING RECENT DELIBERATIONS

The Subcommittee on Medical Economics met on September 13, 1945, to study Senate Bill 1050, the so-called "Wagner-Murray-Dingell Amendment to the Social Security Act."

It was soon obvious that before any critical study of this or any proposed legislation could be made, certain guiding principles on which all could agree should be formulated.

It was also pointed out that Senate Bill 1318, the so-called Pepper "Maternal and Child Welfare Act of 1945," might soon come up in committee and that a study of this bill should take precedence over that of Senate Bill 1050.

It was, therefore, agreed that the committee should

- (1) Outline the important basic principles that were considered essential to a successful medical-care plan
- (2) Prepare a brief discussion of the various methods of payment for medical services
- (3) Study and prepare a critical report on Senate Bill 1318

Subsequent meetings were held on September 27, October 18, November 1, 2, 4 and 19 and December 10 for periods varying from five to seven and a half hours. Drs. Humphrey McCarthy, chairman of the Committee on Legislation, Joseph O'Connor, of Worcester, Stewart Clifford, of Boston, and Caroline Chandler of the State Department of Public Health took an active part in the discussions that followed and were most helpful to the subcommittee. What at times appeared to be widely divergent attitudes were, after free discussion, molded into this report.

The following basic principles were evolved as being essential to a medical-care plan in a free society:

- (1) The objective of adequate medical care in our free society is to make available to everyone—regardless of race, color, creed, financial status or place of residence—every known essential preventive, diagnostic and curative medical service of high quality. The attainment of such medical care must necessarily be an evolutionary process that will require the co-operation of all concerned over a period of years.
- (2) The success of any plan for medical care is dependent on the mutual co-operation of the public, those rendering professional services and the administrative agencies. This co-operation can be obtained only if those rendering the services are convinced that they will have a con-

tinuing authoritative voice in the formulation and execution of policies and plans, thereby assuming their proper share of responsibility.

(3) Provision of adequate medical care for those unable to obtain it by voluntary prepayment plans or by direct payment is the responsibility of the local or state government. Part of the burden of this responsibility may be assumed by charitable agencies. Federal grants-in-aid to state programs administered by state boards of health are an acceptable method of helping to meet this responsibility.

(4) The medical care of those who are able to purchase it by voluntary prepayment plans or by direct payment is the responsibility of the individual.

(5) Eligibility for receiving benefits under a program aided by federal grants should be determined by the individual states.

(6) The patient shall have free choice of his physician, group of physicians, clinic or hospital from among those participating in any plan, provided that the physician, group of physicians, clinic or hospital selected shall have the right to refuse to accept the patient.

(7) Physicians and other qualified persons rendering medical care should receive adequate remuneration for their services. Eventually this should include payment for services rendered to needy patients both in and out of hospitals.

(8) The physician shall be free to elect or reject without prejudice participation in a medical care plan. The rights of the physician as to the choice of methods by which he is to be paid shall be fully protected.

#### *Methods of Paying Physicians Under Medical-Care Plans*

In considering the various methods of paying physicians under such plans, several points must be kept clearly in mind to avoid drawing misleading conclusions from the experience of private practice.

First, in private practice, where the patient pays the bill, there is a deterrent to either excessive demands by the patient or excessive services by the doctor. In any plan where a third party pays the bill, this deterrent is largely removed regardless of the method of payment. Under medical-care plans, provisions against excessive demands should be made by specific clauses in the contracts or by establishing regulatory measures.

Second, under a medical-care program where patients are free to choose their physicians and doctors are free to accept or refuse individuals as patients, the stimulus to the patient and the doctor for establishing a satisfactory relationship is almost independent of the method of payment.

Third, the same opportunity for group practice pertains under any method of payment.

Incidentally, the subcommittee reaffirmed its approval of the Blue Shield prepayment plan spon-

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## HODGKIN'S DISEASE\*

### VI. Clinical Diagnosis

HENRY JACKSON, JR., M.D.,<sup>†</sup> AND FREDERIC PARKER, JR., M.D.<sup>‡</sup>

BOSTON

IN THE last analysis, the diagnosis of any type of Hodgkin's disease must rest on a properly executed biopsy. It is true that in certain advanced cases of Hodgkin's granuloma with generalized lymphadenopathy, evidence of involvement of internal organs, fever, polymorphonuclear leukocytosis and anemia, the diagnosis can be made with some degree of assurance on clinical grounds alone, but even under these circumstances experience has taught us that we may be mistaken.

We therefore advise the removal of a lymph node whenever feasible. The node must be selected with care and with due reference to any possible surgical risks. In all cases, a fair-sized node should be removed, for the small satellites toward the periphery of an involved area not infrequently show merely nonspecific inflammatory changes, and it is not easy to persuade a patient to submit to a second operation for no better reason than that the first one was unsatisfactory. Similarly, a lymph node already subjected to irradiation should be avoided unless there is an express intention to study the results of therapy, for the effect of irradiation is largely cytolytic, and the characteristic cells on which the diagnosis rests may therefore have been destroyed. It is further of the utmost practical importance that the tissue be immediately preserved in a suitable fixative and subsequently be properly cut and stained. The histologic features of Hodgkin's granuloma cannot be identified in poorly prepared tissue, nor, for that matter, can those of any of the malignant lymphomas.

#### GENERAL CONSIDERATIONS

For convenience, the differential diagnosis of Hodgkin's disease may be grouped under three headings: patients with simple localized lymphadenopathy,

those with generalized lymphadenopathy, with or without enlargement of the spleen, and those with constitutional symptoms of one sort or another, associated with little or no enlargement of the superficial nodes.

When confronted with simple lymphadenopathy apparently confined to a single region, one must consider various forms of lymphoma,—that is, giant-follicle lymphoma, reticulum-cell sarcoma, lymphosarcoma, Hodgkin's paraganuloma and Hodgkin's sarcoma,—as well as tuberculosis carcinoma, chronic inflammation, infectious mononucleosis, syphilis, leukemia and certain other conditions.

Without biopsy neither Hodgkin's paraganuloma nor Hodgkin's sarcoma can be distinguished from Hodgkin's granuloma. In the first of these, however, there are few if any systemic symptoms. The peripheral blood reveals no abnormalities, and the patient's general health is at first unaffected. The course is notably long. Most patients with Hodgkin's sarcoma are middle-aged or elderly, the disease being extremely rare under the age of thirty. The patient's health is usually disturbed, often seriously so, even early in the course of the disease. Pain and infiltrative, destructive lesions of the viscera are frequent. Fever and leukocytosis seldom occur except in its terminal stages. The course is rapid, and spontaneous remissions are extremely rare.

Giant-follicle lymphoma is indistinguishable clinically from Hodgkin's granuloma in its early stages except by biopsy.

Reticulum-cell sarcoma occurs in the older age groups, with the significant exception of primary reticulum-cell sarcoma of bone. The involved nodes are usually hard, and sometimes even stony hard, and have a tendency to become fixed to the surrounding tissues. Pain is frequent and often severe. Fever and leukocytosis are rare. Localized reticulum-cell sarcoma is likelier to be mistaken for carcinoma than for Hodgkin's granuloma. This is particularly true when the disease affects the tonsils or the gastrointestinal tract.

\*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard) and the Mallory Institute of Pathology, Boston City Hospital, the Department of Medicine, Harvard University, and the Pondville Hospital, Massachusetts Department of Public Health. This is the sixth of a series of seven papers covering the various aspects of Hodgkin's disease.

<sup>†</sup>Assistant professor of medicine, Harvard Medical School; associate physician, Thorndike Memorial Laboratory, Boston City Hospital; physician, Pondville Hospital, Wrentham, Massachusetts.

<sup>‡</sup>Associate professor of pathology, Harvard Medical School; pathologist-in-chief, Boston City Hospital.

the patient's collection of a cash indemnity rather than for the treatment of illness

Although the amount of administrative paper work concerning medical care would be small, that required by the professional certification of illness might be great

### *The Maternal and Child Welfare Act of 1945*

The Maternal and Child Welfare Act of 1945 (Senate Bill 1318) has been carefully studied by this subcommittee. Although this subcommittee is in complete agreement with the objectives stated in the introduction to the bill, — "To provide for the general welfare by enabling the several states to make adequate provision for health and welfare of mothers and children and for services to crippled children," — it finds serious objections to the bill as written. Some of the more important of these are as follows:

(1) The bill makes no adequate provision for general public-health programs that are more fundamental than this specialized legislation

(2) Services and facilities are available to all who elect to participate, regardless of economic status. This violates Basic Principles 4 and 5

(3) The public deserves a reasonable estimate concerning the ultimate cost of this proposed legislation. Experience and such factual data as are available indicate an ultimate annual budget of approximately one billion dollars. This should be clearly recognized in any consideration of the bill

(4) Fee-for-service method of payment is restricted to consultation or emergency visits and is not ordinarily available to practitioners or specialists

(5) The bill does not make clear just who is to decide the fee for a given service that would be considered adequate remuneration in an individual state, nor does it make provision for variable fees to meet the differing costs in the several states

(6) The bill does not prohibit professional personnel, groups or institutions rendering service under the program from accepting supplemental payment from or on behalf of patients

(7) The bill does not provide for payment to groups of physicians, clinics or hospitals providing professional services

(8) The bill does not emphasize the desirability of full utilization and further development of existing services and facilities

(9) The bill does not emphasize the necessity of restricting the development and expansion of a state program to the capacity of available administrative and professional resources

(10) The bill does not provide the professions rendering service a continuing and authorita-

tive voice in the formulation of policies and provisions of the bill may represent the attitude of the administrator rather than that of a given profession or group. This violates Basic Principle (11). The bill does not provide the facilities whereby the opinions of both the federal and state advisory committees are made available to the public

(12) Designation of the Children's Bureau as an administrative agency does not adequately assure proper integration of the health activities of the federal government

For these reasons we believe that the Maternal and Child Welfare Act of 1945 (Senate Bill 1318) does not represent the best form of legislation for the purposes for which it was written

LELAND S. MCKITTRICK, *Chairman*

## MISCELLANY

### NEW SURGICAL HEAD AT BOSTON UNIVERSITY

Dr. Reginald H. Smithwick has recently been appointed professor of surgery and chairman of the Department of Surgery of Boston University School of Medicine and surgeon-in-chief of the Massachusetts Memorial Hospitals. Dr. Smithwick was formerly associate visiting surgeon at the Massachusetts General Hospital and instructor in surgery at Harvard Medical School. Dr. Smithwick, who is well known for his original contributions to the study and surgical treatment of hypertension and peripheral vascular diseases, will continue and extend his investigations. In this work he will have the close collaboration of the members of the faculty of the Boston University School of Medicine who have been engaged for several years in independent investigations of problems that are closely allied to Dr. Smithwick's studies

## NOTICES

### ANNOUNCEMENTS

Dr. Carlyle G. Flake announces the reopening of his office at 300 Longwood Avenue, Boston, for the practice of diseases of the ear, nose and throat

Dr. Henry A. Kontoff, having returned from active service with the United States Navy, has resumed the practice of urology at 483 Beacon Street, Boston

Dr. Walter S. Levenson, having returned from active service with the United States Navy, has resumed the practice of general surgery at 370 Commonwealth Avenue, Boston

Dr. Abraham Wolbarsht, having returned from active service with the United States Army, has resumed the practice of internal medicine at 375 Commonwealth Avenue, Boston

### SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, January 15, at twelve noon. Dr. Frank A. Pemberton will speak on the subject "The Significance of Bleeding from the Female Genital Tract." Dr. D. D. Hall will preside. Physicians are cordially invited to attend.

(Notices continued on page 37)

Very rarely tuberculosis causes generalized lymphadenopathy. The differentiation of the two cannot be made clinically. The possible confusion of Hodgkin's granuloma with erythema nodosum has already been referred to.

In most cases with systemic symptoms, Hodgkin's granuloma is accompanied even in its early stages by enlargement of superficial lymph nodes, but this may not be so, and in this event the diagnosis can often be made only by exclusion.

Fever may be the presenting and indeed the only symptom for weeks or months, and this sign will later be discussed in detail. Its presence, particularly if it is relapsing in type and is not obviously due to one of the more usual causes, should arouse the suspicion of Hodgkin's disease. A careful search for enlarged lymph nodes especially in the abdomen, should be made, and x-ray studies may reveal the presence of involvement of the mediastinum. One of our patients had a relapsing type of fever for over a year prior to the development of any notable peripheral lymphadenopathy. True relapsing fever due to *Spirillum oberweileri* is practically never seen in this country. Undulant fever may now be diagnosed by appropriate laboratory tests. We have seen a case in which the presence of fever, cardiac murmurs, progressive anemia and a gradually enlarging spleen led to an incorrect initial diagnosis of bacterial endocarditis.

Rarely Hodgkin's granuloma begins with the symptoms of an acute upper respiratory infection — namely, chills, fever and cough. Such cases are almost always rapidly fatal. The tracheo-bronchial and mediastinal lymph nodes, the lungs and the pleura are frequently involved at the apparent onset. Usually, however, there is in addition the telltale superficial lymphadenopathy, either in the neck or in the axilla.

The differential diagnosis of mediastinal masses is always difficult. In our experience, a mediastinal tumor due to Hodgkin's disease is generally associated with enlarged cervical or axillary lymph nodes. The absence of such lymphadenopathy for any great length of time — two to six months — after the demonstration of the tumor is strong evidence that it is not due to Hodgkin's disease.

An adenomatous goiter, particularly if substernal, may cause diagnostic difficulties, for many of the symptoms and signs of hyperthyroidism, such as an increased metabolic rate, tachycardia, sweating, weakness, nervousness and even exophthalmos, may be present both in Hodgkin's disease and in other forms of lymphoma. If the question cannot be decided on clinical grounds, a determination of the organic iodine in the blood<sup>1</sup> will differentiate the two conditions, for in hyperthyroidism the iodine value is two to three times normal, whereas in Hodgkin's granuloma, even with an elevated metabolic rate, it is within normal limits.

Generalized itching, "eczema," weakness without other symptoms, abdominal pain, dyspnea, cough, hematemesis, melena, anorexia, amenorrhea, edema and a host of other nonspecific signs and symptoms testify to the protean character of the disease. In the presence of such symptoms, one can do no more than suspect that Hodgkin's disease is present and search for confirmatory evidence. Since well over 90 per cent of all cases eventually show enlargement of the superficial nodes, an opportunity to prove the diagnosis is usually at hand sooner or later.

#### PERIPHERAL BLOOD PICTURE

##### *Hodgkin's Paragranuloma*

No significant change is seen in the peripheral blood picture in patients with Hodgkin's paragranuloma.

##### *Hodgkin's Granuloma*

Much has been written concerning the changes in the peripheral blood picture of Hodgkin's granuloma. Without question marked deviations from normal are frequent, especially in the late stages of the disease, but when one considers its protean manifestations and the number of organs that are involved, it is not surprising that there is no uniformity of opinion about just what these changes are. Out of the confusing medley of hematologic studies, however, certain facts stand out as being of practical importance. There is no truly characteristic change that is, the disease cannot be diagnosed from a study of the peripheral blood alone.

A variable degree of hypochromic, or more rarely normocytic, normochromic anemia develops in a large proportion of cases, particularly in the late stages of the disease. In approximately one third of our cases — in all of which complete blood studies were done at each visit — the red-cell count eventually fell to 3,000,000 or lower. In 6 patients, 4 of whom were children, it was below 1,000,000. Children seem to be more liable to severe anemia than are adults. In 40 per cent of our patients under the age of twelve years, the red-cell count fell below 2,000,000, in contrast to 13 per cent of the entire group. The pathogenesis of this anemia is uncertain. In some cases it is apparently dependent on involvement of the bone marrow but that this is not invariably so is attested by the facts that in the patient in our series who had by far the most extensive bone lesions the count never fell below 3,600,000 and that in another patient who had a terminal count of 500,000 there was no evidence of bone involvement. In rare cases,<sup>2,3</sup> there is hemolytic anemia of considerable severity, simulating in some respects, in so far as the peripheral blood is concerned, that of a congenital or acquired hemolytic anemia. In many of these cases there is a pseudomacrocytosis due to the presence of an increased number of reticulocytes. There may or

Lymphosarcoma, which is oftenest seen in childhood and in late adult life, is extremely rare between the ages of twenty and thirty years, a period of life during which Hodgkin's granuloma is frequent. The involved nodes that are the peripheral expression of lymphosarcoma are usually rather soft and tend to be of uniform size and distribution. Fever is rare except in the forms of the disease associated with acute lymphatic leukemia, in which it may be the most prominent symptom. The blood however, frequently shows an increased percentage of lymphocytes, even in the absence of frank leukemia. Leukemia often accompanies lymphosarcoma or follows its development in children but is less frequent in adults.

Tuberculosis is extremely difficult to distinguish from Hodgkin's disease of any type, and it must be remembered that the two diseases occasionally occur in the same patient and, indeed, rarely in the same node. Redness of the overlying skin, fluctuation, caseation and sinus formation are not infrequent in tuberculosis, whereas they are extremely rare in Hodgkin's disease. It has been said that tuberculosis is prone to involve nodes in the anterior triangle of the neck, whereas Hodgkin's granuloma usually affects those of the posterior triangle, but this rule is treacherous. In our experience, large single nodes in the cervical or axillary region are likely to be tuberculous. The tuberculin reaction is usually positive in the presence of tuberculous lymph nodes, whereas it is almost always negative—even in high concentrations—in untreated Hodgkin's granuloma.

The presence of parenchymal disease of the lung should not be taken as proof that the entire process is tuberculous, for the pulmonary lesions of Hodgkin's granuloma may closely simulate those of tuberculosis, and the two diseases may coexist in the same person. Similarly, one should not be led astray by a past history of tuberculosis. Not infrequently proved tuberculous lymphadenopathy in childhood is followed by Hodgkin's granuloma in early adolescence or later life. The differentiation of these diseases can be easily made by biopsy.

Carcinomatous nodes are generally stony hard and are often fixed to the adjacent tissues, whereas the nodes in Hodgkin's granuloma, unless they have been heavily irradiated, are at most extremely firm. Carcinoma is likelier to cause pain, and the primary focus may be discovered and be patently cancerous. It must be remembered, however, that lymph nodes involved by rapidly growing carcinoma or sarcoma may be even softer than those of Hodgkin's granuloma, and that under these circumstances a clinical differential diagnosis may be impossible.

Chronically inflamed nodes secondary to a focus of infection that is often not obvious are not infrequently seen in children but are rare in adults. Small, pea-sized, painless, freely movable superficially situated nodes are, of course, often found

in the cervical and inguinal regions of many healthy adults. Their presence need cause no necessary alarm, but the persistence of a notably enlarged node or group of nodes especially if they are painless and fluctuate in size, calls for careful consideration whether a biopsy should be done. If there is any doubt, a node should be removed and the uncertainty thus removed. If there is only chronic inflammation, little has been lost, if the histologic picture is that of Hodgkin's granuloma, time has been gained. It must be constantly borne in mind that in many cases nodes affected by Hodgkin's granuloma fluctuate remarkably under the influence of coincidental nearby infection, and that the subsidence or even the virtual disappearance of cervical nodes should not be taken as proof that they merely represent chronic inflammation. This point is well illustrated by the following case.

R.S. (P13671), a 19-year-old girl, whose father had died of tuberculosis when she was a small child, in 1933 noted painless lymph nodes in the left side of the neck. For the next 5 years, these fluctuated greatly in size and varied in number, diminishing during the summer months and increasing during the winter particularly with the occurrence of upper respiratory infection.

In January, 1938, the patient developed a severe "cold" and the nodes increased greatly in size. There was some cough and considerable dyspnea, but there was no disturbance of the general health or loss of weight. A node was excised and showed the typical picture of Hodgkin's granuloma. X-ray studies revealed the presence of a small mediastinal tumor.

Whether the nodes observed in 1933 were actually the site of Hodgkin's disease must, of course, remain an open question. Earlier biopsy would have decided this point, and earlier treatment—had the nodes been granulomatous—might have aborted the disease.

Infectious mononucleosis occasionally simulates Hodgkin's disease. Usually, however, the diagnosis is clarified by the peripheral blood picture and is substantiated by the heterophil agglutination test. Rarely the lymphadenopathy and splenomegaly of infectious mononucleosis remain for months after the subsidence of the acute disease. Under these circumstances, a careful history is important, and biopsy may be necessary.

Syphilis should cause no confusion if due attention is paid to the history and to the appropriate laboratory tests. We have seen a case, however, in which following a frozen-section diagnosis of lymphosarcoma a breast amputation and axillary dissection were done, the patient proving to have secondary syphilis. Parenthetically, it may be said that in malignant lymphoma a frozen section is an extremely slender reed on which to lean.

Lymphatic leukemia, rare in the twenties and thirties, is accompanied by the characteristic peripheral blood picture.

Rarely myelogenous leukemia is accompanied by generalized lymphadenopathy or enlarged nodes in a single region. The characteristic blood picture should make the differential diagnosis clear.

area Too often such lymphadenopathy is regarded as due to the infection alone, it is too infrequently recognized that lymph nodes involved by Hodgkin's granuloma but not greatly enlarged may rapidly increase in size after what appears to be a simple infection

There is a peculiar and characteristic reaction that deserves special attention — so-called "Pel-Ebstein fever" In 1887, Pel<sup>6</sup> and Ebstein<sup>7</sup> independently described a relapsing form of fever characterized by periods of pyrexia, alternating with intervals during which the temperature is normal or subnormal The febrile periods are marked by a gradual daily increase in temperature to 104°F or more and a subsequent equally orderly decline to normal The pulse and respirations usually follow the temperature in such a manner that when the latter is 104°F the pulse is 120 to 150 and the respirations are 30 to 35 During the period of increased temperature, most patients feel extremely ill There follows an afebrile period of weeks or months, during which the patient may return to apparently perfect health, but sooner or later the fever returns and the afebrile intervals become shorter, and eventually the fever becomes continuous

This syndrome, although usually referred to as Pel-Ebstein fever, was accurately described by Murchison<sup>8</sup> in 1870 in a case of so-called "lymphadenoma"—the British term for Hodgkin's granuloma By rights, if any man's name is to be attached to the syndrome it should be Murchison's

Mac Nalty<sup>9</sup> has made a special study of the fever in Hodgkin's disease

The following case is illustrative of Pel-Ebstein (Murchison) fever

F C (P2903), a 22-year-old house painter, entered the hospital on January 20, 1931 In the spring of 1930, he noted a painless lump the size of a walnut in the left side of the neck This was removed at another hospital and showed the usual histologic picture of Hodgkin's granuloma At that time there were no other symptoms, and the patient was lost sight of In October, 1930, he began to have attacks of fever, malaise and anorexia These lasted for 10 days or so and recurred after an interval of apparent good health, about every 6 weeks During each attack the patient was confined to bed and extremely prostrated, but between attacks he felt perfectly well Each febrile episode was ushered in by a marked sense of drowsiness and anorexia, and the temperature rose higher each night until by the end of 5 or 6 days it had reached 104 or 105°F It then gradually subsided to normal by about the 15th day During the febrile period there was marked anorexia, sweating and extreme prostra-

tion As soon as the temperature became normal the patient again felt quite well and was able to resume his daily work

Physical examination on entry showed no abnormalities except for a small scar in the left side of the neck An x-ray film of the chest showed a slight increase in the mediastinal shadow There was slight anemia The white-cell count was normal but the differential count showed 90 per cent polymorphonuclear leukocytes and 10 per cent lymphocytes

Following x-ray therapy to the chest the small mediastinal mass disappeared, but there was no symptomatic improvement, and the patient continued to have recurrent attacks of fever, malaise, extreme weakness, anorexia and fleeting generalized pains The intervals between attacks constantly became shorter, and the fever finally became continuous X-ray therapy had no effect, and Fowler's solution in large doses caused no improvement

Four months after entry, the liver and spleen became palpable One month later, jaundice appeared and the spleen reached the umbilicus, but there was still no peripheral lymphadenopathy Anorexia was extreme and loss of weight very marked, and drowsiness became a more and more prominent feature The patient's strength rapidly failed, and he died on April 17, 1931, about 7 months after the onset of the generalized symptoms and 1 year after the first symptom of painless lymphadenopathy

Autopsy Post-mortem examination showed widespread Hodgkin's granuloma, with scarcely an organ spared The main lesions were chiefly in the liver, the spleen and the retroperitoneal and mediastinal lymph nodes

Uddströmer<sup>5</sup> found this type of fever in 7 per cent of his cases, in our series it was present in 5 per cent

*Hodgkin's Sarcoma*

Fever occurs in approximately one third of the cases of Hodgkin's sarcoma, although it follows no particular pattern and is rarely very high, not infrequently, however, one sees a septic type of temperature reaching a daily peak of 102°F Pel-Ebstein (Murchison) fever does not occur Definite chills are occasionally seen, and in patients having them the prognosis is extremely bad We have never had such a patient who lived more than two years after the apparent onset of the disease

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may not be alteration in the fragility of the red cells. The exact explanation of this hemolytic anemia in Hodgkin's granuloma is yet to be determined.

It is generally agreed that although the white-cell count is rarely normal throughout the disease, leukocytosis is extremely frequent, and that, on the other hand, extreme leukopenia may occur. Sixty-three per cent of our patients had a white-cell count of 11,000 or over. In 12, the count was at one time or another above 25,000. The leukocytosis occurs quite independently of fever. Marked leukopenia occurred in 12 per cent of the cases. There seemed to be no correlation between the clinical findings and the leukopenia, but in certain cases the latter seemed to be due to irradiation, especially when this had been applied to the abdomen. Marked fluctuations in the white-cell count may occur within a short period of time and without apparent cause.

Certain significant changes take place in the differential white-cell count. By far the most constant one is a relative or absolute increase in the percentage of polymorphonuclear neutrophils, a point on which all investigators are agreed. In 81 per cent of our cases, this percentage was at one time or another over 75, in 5 cases, it was 95 or more. This change tends to become increasingly more pronounced as the disease advances. There is a strong tendency toward a shift to the left, and myelocytes in varying proportions are not rare. They were found, usually in small numbers and inconstantly, in 11 per cent of our cases.

An occasional case shows an increased number of eosinophils. Baldridge and Awe<sup>4</sup> report a case with a white-cell count of 43,000 and 83 per cent eosinophils. Uddström<sup>5</sup> found over 6 per cent eosinophils in only 12 per cent of his cases, and was unimpressed either by the importance of eosinophilia in the disease or its relation to itching, which has been stressed by many writers. In our experience, marked eosinophilia is rare, and when one recalls the large variety of conditions accompanied by an increase of these cells, it seems not improbable that in certain cases, at least, the eosinophilia is unrelated to the Hodgkin's granuloma.

Monocytes are frequently increased in number, and in rare cases greatly so.

The number of platelets shows no constant change, although they are not infrequently moderately increased.

In summary, the most frequent blood changes in Hodgkin's granuloma are a normochromic or hypochromic anemia, a moderate increase in the white-cell count and a moderate to great increase in the percentage of polymorphonuclear neutrophils.

#### *Hodgkin's Sarcoma*

A moderate degree of anemia—usually hypochromic, occasionally normocytic and rarely macro-

cytic—is seen in Hodgkin's sarcoma. In only a small percentage of the cases, however, does the anemia become extremely marked. In 5 of our cases, the red-cell count was below 2,000,000, with a correspondingly low hemoglobin. One of these patients may possibly have had a hemolytic type of anemia, for the icteric index was 50 and there was nothing to account for the jaundice. Fragility tests were not done, however, so that one cannot be categorical on this point.

The white-cell count is usually normal, rarely it is moderately elevated. The percentage of polymorphonuclear neutrophils is almost invariably high, and in approximately one third of the cases there is a marked increase in the percentage of monocytes. Myelocytes occasionally occur.

There seems to be no correlation between the hematologic findings and either the organs involved or the course of the disease.

#### FEVER

##### *Hodgkin's Paragranuloma*

In patients with Hodgkin's paragranuloma, fever does not occur.

##### *Hodgkin's Granuloma*

Fever of one type or another, unaccompanied by sepsis or incidental and unrelated infectious diseases, is an extremely frequent finding in Hodgkin's granuloma. Uddström<sup>5</sup> in Sweden reported that fever was present in 54 per cent of 484 collected cases. In our series, it occurred at one time or another in at least 43 per cent, it is probable that the incidence would have been higher if every patient had been constantly observed throughout the course of the disease.

The fever may be of various sorts. Most frequently it is, as Uddström puts it, "typeless." Occasionally it is intermittent or remittent, reaching 101 to 105°F every day. More rarely a high continuous fever is seen. Such a finding is almost always terminal. It is common knowledge that pyrexia becomes increasingly frequent as the disease advances.

During febrile periods unassociated with sepsis it is usual for the lymph nodes to increase in size, splenomegaly, if it exists, frequently becomes more marked, and the patient is generally prostrated, weak and debilitated. Tachycardia, sometimes extreme, almost invariably accompanies the fever. Occasionally, however, one sees a patient who, in spite of a moderate increase in temperature—99 to 101°F—feels perfectly well and is, indeed, unaware of any febrile reaction, and the fact that peripheral lymphadenopathy is absent or inconspicuous at the time may render the correct diagnosis extremely difficult.

Infections, particularly those affecting the upper respiratory tract, are prone to cause coincident enlargement of lymph nodes close to the affected

classified as a psychoneurosis. To say that these patients are not psychiatric cases because there is no name for them except "gold brickers," "inadequate personalities" or "opportunists" is to neglect a serious problem, for the number of hospital beds occupied by this type of patient is large, and will be proportionately larger in veterans' hospitals after the war.

The definition under discussion need not exclude patients who suffer from some organic disorder but whose incapacitating symptoms are primarily nervous or emotional. It is evident that many situational and symptomatic disorders of this kind masquerade under such terms as "gastritis," "colitis," "effort syndrome," "myositis," "rheumatism," "eye strain," "neuritis" and "neuralgia" — to mention only a few. The inefficiency and failure of many of these persons are frequently more closely related to emotional instability or lack of tolerance of the military situation than to defective functioning of the organ in question. This broad definition of nervous breakdown may be objected to as being all-inclusive, and it is admitted that there are many men on the wards in military hospitals who would probably never consult a physician in peacetime, unless it were to obtain an excuse for inability to carry out life's obligations in a satisfactory manner. Such patients' disability or failure in performance is largely one of loss or lack of morale. They constitute casualties fully as much as do men with wounds, and in addition they have a much more damaging influence on the morale of the group to which they belong.

The retreat of the British from Mons in World War I is cited as an instance of stress so severe that many broke under the strain.<sup>1</sup> One should, however, not lose sight of the fact that appreciable numbers did not break down — notably those who stood, fought and won in the Second Battle of the Marne. In this war it would be of considerable interest and value to know the actual percentage of nervous breakdowns among those who were evacuated at Dunkirk, among the men who fought on Guadalcanal or among the troops engaged at Stalingrad, Anzio, Dieppe, Tarawa and Iwo Jima. If one happens to see a large number of neuropsychiatric patients from the same combat zone, one is apt to conclude that these casualties were unusually high, whereas actually one may know little of the total number of troops involved.

One cannot base a diagnosis of mental disorder entirely on the symptoms presented. The patient's attitude toward them is far more important than their degree of severity. One sees many men returning from combat or operational duty and many survivors of ship sinkings who are anxious to carry on in the face of distressing somatic symptoms. This has been observed both in officers and among the enlisted personnel. The essential feature seems to be a high morale or sense of duty, dependent

primarily on the stability of the personality prior to entry into the service. The presence or absence of morale in an individual or a group is a complicated matter. Morale depends on many factors, two of which appear to be of outstanding importance. One is the inherent emotional stability of the person, the other is his quality of leadership or confidence in leadership. There are many men with a defective emotional adjustment who are held in line by the *esprit de corps* of the group, being profoundly influenced by leadership, who break down when this protective influence is removed or regain their morale if effective leadership is provided. It must be borne in mind, however, that a large percentage of men in a given unit do not break down mentally, irrespective of what may happen to their leaders. It is true that the military effectiveness of any unit may be gravely influenced by a relatively small percentage of casualties of whatever type, and particularly by mental casualties. If competent, skilled and resourceful leaders take over such a demoralized unit, their task is not so hopeless as might appear at first glance, since they are dealing with a group that has had its most unstable men screened out by exposure to combat, so that those who remain, together with replacements, have not had nervous breakdowns. This is not meant to detract in any way from the role of leadership in producing an effective fighting unit or to oversimplify the problem of the maintenance of morale. It is intended only to point out that at times too much attention is focused on the man who breaks down mentally. An entire unit may be branded as "NP" or "psycho" even though the unit has a relatively low mental-casualty rate, the men who have stood up under all kinds of trying circumstances being lost sight of. The emotionally unstable are evacuated to safer zones and are eventually returned home, the majority being discharged from the service with varying degrees of disability. For the larger percentage of men who did not break down, "Valor-like virtue is its own reward" and may turn out to be a reward full of bitterness in the postwar period, if society fails to provide adequate opportunity for the veterans who are chiefly responsible for the winning of the war.

It has been the practice at this center, when examining sailors from various fighting ships or marines who had been through a strenuous campaign, to ask whether they knew of anyone aboard their ship or in their outfit who broke down mentally. The questions were asked both of men who showed evidence of emotional disorder and of those who did not. The replies appear to be of some significance. Without exception these men knew of only one or two others who had suffered a breakdown, and in some instances an entire ship's crew or company of marines had no psychiatric casualties.

It is realized that this method of acquiring data will not bear critical evaluation, since a fair number

## MENTAL BREAKING POINTS\*

COMMANDER JOHN B. DYNES (MC), USNR †

IF THE psychiatrist interviews servicemen who have broken down mentally day after day, month in and month out, he is likely to conclude that all men have mental breaking points, furthermore, he may wonder how it is possible that the United States is winning the war. His outlook on life and his interpretation of human behavior are apt to be colored, if not strongly influenced, by the symptoms and diseases that he finds in his patients. It is evident that all patients referred to the psychiatrist in a military hospital must have mental symptoms of some type. To decide that all men have mental breaking points on the ground that all those whom the psychiatrist interviews have shown one, or have had nervous breakdowns, appears to be drawing general conclusions from an extremely small and badly chosen sample.

In the past year the popular press has issued many warnings and even appeals to the public, and in particular to the families and friends of servicemen, on what to do or say, or what not to do or say, when veterans come home. Most of this advice is sincere but misdirected. If applied to those who have developed nervous or mental disorders it might be of more value, although one should avoid generalizations and should treat each man according to his needs. The reaction against this type of advice among men in the service who are in good physical and mental health is in many cases one of resentment and annoyance. It is believed that the basic reason why the majority of returning veterans are disturbed by the special treatment accorded them by their family and friends is that they are getting the treatment intended, not for them, but for the psychiatric war casualties, among whom they do not belong.

Why should this error occur? The explanation is thought to lie in the belief or theory, held by laymen and by physicians alike, that all men have mental breaking points or can take only so much, or, to put it another way, that all men are apt to "crack up" or have a nervous breakdown if the stress of combat or military life is severe enough.

One not infrequently hears such a remark as "It was more than he could bear," "A man can only take so much," or "He couldn't take it any longer." These statements are widely used by laymen to denote a nervous breakdown in the face of overwhelming misfortune or severe environmental stress. The emphasis is frequently placed on "an unkind fate" or on "outrageous fortune," over which the individual has no control. The victim

is supposedly caught in the toils of circumstance and irresistibly crushed. Since World War I considerably more attention has been paid to the individual than to the environmental stress, and there appears to be an unofficial but fairly general agreement among psychiatrists in the armed forces that the stability of a man's personality prior to entry into the service is more important in the maintenance of mental equilibrium than is the severity of the combat stresses to which he may have been subjected.

Obviously, the terms "breakdown" and "breaking point" have physical and mechanistic origins and are used only metaphorically — but nevertheless effectively — in referring to mental disorders. Such terms as "stress," "tension," "pressure," "weight," "force" and "impact" have been borrowed because they are descriptive, and because analogies can be easily drawn, supported or reinforced by their use. Psychiatrists use the term "nervous breakdown" with caution, preferring some such descriptive or diagnostic term as "psychoneurosis," "dementia praecox" or "psychopathic state" — to mention only a few of these — denoting the character or trend of the disorder. These terms are labels, at times hardly more satisfactory — and certainly more confusing to the layman — than "nervous breakdown." It is evident that any expression of this kind must be related to some frame of reference that indicates inefficiency or failure in performance, such as unfitness for military duty, for life in the community — involving mental institutionalization — or for work. In each case the essential element is a failure of performance or loss of efficiency for the task assigned, which may vary both qualitatively and quantitatively. For practical purposes in this paper, the term "nervous breakdown" refers to such failure of efficiency that is directly or indirectly related to an emotional or mental instability that necessitates medical care. So long as such a man remains a patient in a medical unit, he is an ineffective person so far as the military service is concerned.

Such a definition of nervous breakdown obviously includes a wide range of mental disorders, from low morale, with its aversion to fighting and hardships, to major psychoses. It is also applicable to those self-centered persons who are feigning or exaggerating various somatic complaints to escape military duty. It is evident to many neuropsychiatrists working in military hospitals that a great many patients on medical, surgical and psychiatric wards suffer from a certain lack of morale or failure in performance that is not dependent on unconscious mental conflicts and should certainly not be

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†Instructor in psychiatry, Harvard Medical School, and neuropsychiatrist, Lacey Clinic, Boston (on leave of absence).

retained have repeatedly proved themselves to have stable personalities

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It is obvious that not all men suffer mental breakdowns under severe stress. It is not meant to imply that the human organism is indestructible, since physical exhaustion and organic disease are bound to take their toll, or that a person under prolonged and severe stress may not fail in some manner other than mental. To argue whether a stable personality develops a nervous breakdown if just the proper set of stresses happen to strike at the same time is profitless. But this is not a question of practical importance, since experience shows that the great majority of fighting men are capable of absorbing the shock of all the blows to which they are subjected without showing signs of a nervous breakdown.

It would be erroneous to judge the mental health of all men under arms by the picture presented on the neuropsychiatric wards of military hospitals. It would be just as erroneous to assume that the 10 men out of 2000 cited above represented all

those who may subsequently break down mentally under service conditions. It is apparent that men with stable personalities are much less susceptible to the stress of military service in wartime than are those having poorly balanced or defective personalities. It is principally the man with a defective or maladjusted emotional life who is likely to break mentally under the stress of military duty, and although it is generally believed that even the most stable personality may crack under the strain of combat, this state of affairs is exceedingly rare. All that can be said with certainty is that only those who actually break have mental breaking points, and that experience, at a naval receiving station in examining men fresh from combat and noncombat duty and survivors of ship sinkings does not support the widely accepted theory that all men have mental breaking points.

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### THE INCIDENCE OF LEUKEMIA IN RADIOLOGISTS\*

HELMUTH ULRICH, M D †

BOSTON

EXPOSURE to x-rays has for some time been regarded as a possible cause of leukemia. This belief is based in part on results obtained by experimental exposure of animals to x-rays<sup>1-4</sup> and in part on several reports of cases of leukemia occurring in workers exposed to radiation.<sup>5-15</sup> Definite proof of such an etiologic relation has not been established, however, and some authors have expressed doubt concerning it. Thus, Evans and Roberts<sup>8</sup> stated in 1928, after a review of the literature to that date, "Although the possibility of causal association cannot positively be denied, the evidence is not conclusive." Haagensen<sup>9</sup> wrote, "Doubt may be raised as to the relationship of the exposure to radiation and the development of leukemia," and Warren and Dunlap,<sup>16</sup> in their comprehensive review published in 1942, stated "Few examples of leukemia have been described in persons chronically exposed to radiation. Only 24 case reports are found in the literature if one excludes all reports of leukemia following the therapeutic irradiation of lymphatic tumors."

More recently, Henshaw and Hawkins,<sup>17</sup> having found that none of the existing evidence furnishes any direct proof that radiation actually acts as a carcinogenic agent in the induction of leukemia in

human beings, determined the incidence of leukemia in physicians from the death notices published weekly in the *Journal of the American Medical Association* and compared it with similar data regarding the general population, derived from the vital statistics of the United States Bureau of the Census. They found that during a ten-year period (1933-1942) 0.53 per cent of physicians died of leukemia, as compared with 0.39 per cent of the general population. After making corrections for differences of age, sex and other factors that influence the outcome, they arrived at the following conclusion: "Leukemia was recognized approximately 1.7 times more frequently among physicians than among white males in the general population." They stated that, although these observations furnished no direct proof that radiation acts to incite leukemia in human beings, they were nevertheless in accord with the findings on experimental animals in which exposure to x-rays had been found to increase the incidence of leukemia.

Since the majority of physicians are not subject to exposure to radiation, it seems that a comparison of the incidence of leukemia among radiologists and that among other physicians should give more conclusive results. The present report is based on a statistical study of deaths of physicians reported in the *Journal of the American Medical Association* during the ten-year period 1935-1944.

\*From the Department of Internal Medicine, Boston University School of Medicine, and the Department of Internal Medicine, Massachusetts Memorial Hospitals.

†Associate professor of medicine, Boston University School of Medicine.

of men have a delayed reaction and may not develop their mental disorder until later, and since the casual observer is apt to mistake the true diagnosis in certain cases or to misinterpret unusual behavior. It is, however, not necessary to rely on such hearsay, particularly when more reliable information is available. The psychiatrist at a naval receiving station has an unusual opportunity of interviewing all the survivors of sunken ships and all men returning from combat or naval operations. The type of screening thus accomplished is unlike any other, but most closely resembles that done at induction centers, with an important difference: all men interviewed had been subjected to the test of combat or overseas duty. It can hardly be said that they had not been subjected to the type of stress that precipitates a nervous breakdown in susceptible persons.

The significant fact concerning these men returning from overseas is that so few of them showed any evidence of emotional instability or nervous breakdown. The great majority declared that they had never experienced any disabling nervous symptoms, even though many had been in combat on a number of occasions. It was true that the majority admitted that they had experienced fear and its attendant autonomic symptoms, but exceptionally few had been incapacitated by fear.

Two thousand men were given a questionnaire, the Cornell Selectee Index,<sup>2</sup> a short psychiatric or psychosomatic inventory consisting of sixty-four questions designed to elicit evidence of emotional instability. In addition, each man was interviewed. Of these 2000 men, 500 were survivors of sunken ships, 1000 had returned from combat duty, and 500 were being returned from overseas duty. Many of the latter from advanced outposts, where the stress of military duty is said to be even more trying than that of actual combat. Only 10 showed evidence of nervous breakdown according to the definition given earlier in this paper. These men showed evidence of emotional instability, with an increased startle reaction, increased fatigability, tremors, palpitation, insomnia, nightmares, headache, irritability, gastrointestinal disturbances, anxiety and depressive reactions, severe enough to render the victim unfit for military duty and to warrant sending them to a naval hospital.

Table 1 shows the percentage of each group of men giving twenty-five or more positive answers. It is claimed that this method of scoring screens those having a severe degree of emotional maladjustment. It is of interest that although 5 per cent of the 2000 men showed evidence of severe nervous symptoms, all but 10 of these had been able to serve in the armed forces overseas without developing evidence of a nervous breakdown. It would be erroneous to assume that these 90 men had been missed in answering this index. Personal interviews ruled out this factor and established a previ-

ously mentioned principle, namely, that symptoms alone are not indicative of a nervous breakdown, the subject's attitude and reaction toward them being far more important than their severity.

This low percentage of men with a significant nervous disorder was at first somewhat startling, since the psychiatrist had rarely had an oppor-

TABLE 1 *Cornell Selectee Index Scores of Returned Personnel*

GROUP	NO OF MEN	PERCENTAGE WITH SCORES OF 25 OR MORE
Men returned from combat duty	1000	6
Men returned from noncombat duty	500	6
Survivors of sunken ships	500	4
Total	2000	
Hospitalized for nervous breakdown	10	100

tunity to interview men who had been through combat or the prolonged stress of trying overseas conditions and had continued to maintain their mental equilibrium. It may be argued that a certain number of men had been hospitalized for nervous disorders prior to the return of their units to this country, and also that some of those interviewed may be expected to develop disabling nervous symptoms many weeks or months after their experience, but even allowing for these cases, the percentage of men who develop a nervous breakdown under the stress of military service is extremely small if compared to the total number in the service. This group of psychiatric war casualties should be adequately cared for, and those familiar with the military services know that such rehabilitation programs are under way at the present time.

It is believed that there has been considerable overemphasis on the serious consequences to the man who has been in combat or under the prolonged stress of military operations. It is not the intention of this paper to minimize the important work done by psychiatrists in the detection, elimination and care of psychiatric war casualties. It is thought, however, that a complete over-all picture of the mental health of the men in the armed forces is not reflected by the reports in the popular press nor by those emanating from military hospitals, for it is evident to psychiatrists serving in such military activities that they see only those who have broken down mentally or have failed in the performance of their duty, and thus tend to lose their perspective regarding the mental health of all men under arms. It should be apparent that even though the definition of nervous breakdown given above is broad, the percentage of men in the service who have had such a disorder is relatively small.\* This is due in part to the excellent work done by psychiatrists at induction centers and training stations—frequently working under considerable handicap—in the elimination of the psychiatrically unfit. The great majority of those

\*Estimated 5 per cent at the maximum.

## ICE CREAM AS A SOURCE OF RIBOFLAVIN, CAROTENE AND ASCORBIC ACID\*

ARTHUR D HOLMES, PH D,† JOHN W KUZMESKI, B S,‡ CARLETON P JONES, M S,§  
AND FRANK T CANAVAN¶

AMHERST, MASSACHUSETTS

MANY people consider ice cream as a luxury food, a dessert or an attractive adjunct to teas and other social occasions where light refreshments are served. Consequently this food does not ordinarily receive proper recognition as a valuable source of protein, fat carbohydrate, minerals and vitamins all of which are essential dietary constituents. In fact most people fail to realize the extent to which ice cream is consumed in this country. It is reported that 412,144,000 gallons were used during 1943,<sup>1</sup> or over 3 gallons for every man, woman and child. It is difficult to estimate accurately the retail value of this ice cream, since large quantities are retailed in cones of various sizes and as individual servings at stores and resorts, but on the basis that ice cream retails for 75 cents a quart, the retail value of ice cream consumed in 1943 amounted to at least \$1,236,432,000. This is about one fourth the retail value of the whole milk and over twice the retail market value of the eggs, apples or potatoes consumed annually.<sup>2</sup> A survey of the literature, however, failed to reveal much information concerning the vitamin content of this valuable food, and this study was conducted to accumulate data in this connection.

## PREPARATION OF ICE CREAM

The coffee, maple and vanilla ice creams used in this study were made at the Dairy Manufactures Laboratory, under the conditions maintained for training students and for the preparation of ice cream for the Massachusetts State College dining halls. The ingredients for 100 pounds of ice-cream mix were 24 1/4 pounds of cream (40 per cent), 56 3/4 pounds of whole milk, 15 0 pounds of cane sugar, 4 0 pounds of skimmed milk powder, and 0 3 pounds of gelatin. The whole milk and cream were produced by the college herd of Avyrshire, Guernsey, Holstein, Jersey and Shorthorn cows fed and maintained under conditions similar to those of local progressive commercial dairies.

The ingredients were thoroughly mixed and pasteurized by the holding method at 145°F for thirty minutes. When pasteurization was completed, the mix was passed through a homogenizer at 145°F under 2500 pounds pressure per square inch to break up the fat globules and obtain a product of uniform composition. The ice-cream mix was cooled to 40°F and allowed to blend or ripen

for eighteen hours. At this stage of manufacture, the ice cream weighed 9 25 pounds per gallon. The mix was then placed in a batch freezer, and flavoring was added at the rate of 6 ounces of vanilla, 32 ounces of coffee extract or 12 ounces of imitation maple flavor per 100 pounds. During the freezing process the flavoring was intimately incorporated and sufficient air was whipped into the mix so that the final ice cream weighed 5 pounds a gallon. Thus, essentially half the volume of the finished ice cream consisted of occluded air. The finished ice cream was placed in commercial 4-ounce cardboard containers and held in a refrigerator at -10°F. This ice cream was not strictly comparable to the present-day wartime commercial product, since the latter ordinarily contains only about 10 per cent of fat, whereas the ice cream used in this study contained 12 per cent of fat.

## ASSAY PROCEDURES

*Carotene*

The carotene content of the ice cream was determined by a modification of the method of Boyer, Spitzer, Jensen and Phillips.<sup>3</sup> Briefly, the procedure was as follows. A 20-gm sample of ice cream was extracted with 30 cc of alcoholic potassium hydroxide solution—40 gm of potassium hydroxide completely dissolved in 50 cc of distilled water and thoroughly shaken with 180 cc of ethyl alcohol—and allowed to stand for three hours. Twenty-five cubic centimeters of diethyl ether was added and the mixture was vigorously shaken for one minute. After the second extraction with ether, the two extracts were combined, 25 cc of Skellysolve B was added, and the mixture was vigorously shaken for fifteen seconds. Twenty-five cubic centimeters of 80 per cent methyl alcohol was added and the mixture was shaken for one minute. The alcohol-water-ethyl ether layer was discarded. Fifty cubic centimeters of 3 per cent sodium sulfate solution was added and the mixture was vigorously shaken four separate times. The water layer was discarded. Ten cubic centimeters of Skellysolve B was added and the Skellysolve layer was filtered through No 41 Whatman filter paper containing about 5 gm of anhydrous sodium sulfate into a 50-cc amber flask. The separatory funnel was rinsed with Skellysolve, and the filter paper and sodium sulfate were washed with separatory rinsings until a volume of 50 cc had been reached. The regular procedure was then followed.

*Riboflavin*

The following procedure was used to determine the riboflavin content of ice cream. Ten grams of ice

\*Contribution No 565 of the Massachusetts Agricultural Experiment Station

†Research professor in chemistry, Massachusetts State College.

‡Senior chemist, Control Service, Massachusetts State College.

§Assistant research professor in chemistry, Massachusetts State College.

¶Superintendent, Dairy Manufactures Laboratory, Massachusetts State College.

It must be admitted that the results cannot be perfect, first, because, as indicated by Henshaw and Hawkins,<sup>17</sup> the cause of death is not given in about 25 per cent of the obituary notices, and second, because in an even greater number there is no indication of possible x-ray exposure. For example, some of the physicians not listed as radiologists but dying from leukemia may have been exposed to radiation, — the case reported at the end of this article is of this type, — which would increase the incidence of leukemia in the exposed group. Conversely, some unexposed physicians, the cause of whose death is not given, may have died of leukemia, which would increase the incidence in this group. It is not unreasonable, therefore, to assume a tendency of the various unknown opposing factors to balance each other. At any rate, if the difference between the two groups is sufficiently large, it should not be significantly affected by these discrepancies.

From 1935 to 1944, inclusive, the deaths of 34,626 physicians were recorded in the *Journal of the American Medical Association*. Two hundred and five of these men were listed as radiologists. The total stated number of deaths from leukemia is 158. Eight of these occurred among the 205 radiologists, giving a percentage of 3.9, 150 were among the 34,421 physicians not listed as radiologists, a percentage of 0.44. Therefore, those known to have been exposed to radiation had an incidence of leukemia more than eight times as great as those who are not listed as radiologists. Although this difference may be affected somewhat in either direction by the previously discussed lack of complete information, it seems too great to be wiped out or to be significantly modified.

This statistical study, which supplies substantial evidence that exposure to radiation is a potential cause of leukemia, was suggested by the occurrence of this disease in a physician who had repeatedly been exposed to radiation over a long period of time. The following data summarize the findings in this case.

R. J., a 51-year-old dermatologist, had for several years failed to take precautions against exposure to radiation that he used for treating his patients. Symptomatically his illness began in the fall of 1941, the major complaint consisting of pain in various parts of the body, especially in the chest. It became quite severe during a period of 6 weeks and was aggravated by motion and deep respiration. Slight fever (99.2°F) was present. The skin was pale and suggested anemia, which was confirmed by examination of the blood, the red-cell count being 2,610,000 and the hemoglobin 45 per cent. Leukopenia was present, the number of leukocytes varying between 1500 and 5540 per cubic millimeter and the percentage of neutrophils between 4 and 54. The lymphocytes, largely normal in appearance, were the most numerous leukocytes in the majority of smears. At times occasional immature cells of the lymphoblastic type were found. The leukopenic blood picture persisted essentially unchanged for 6 months, when the total number of leukocytes began to increase and reached a maximum of 163,200 within 2 weeks, with a differential count typical of lymphatic leukemia. The patient died on August 20, 1942, approximately 9 months after the onset of symptoms. Autopsy confirmed the diagnosis of lymphatic leukemia.

This case is intentionally omitted from the group of 8 cases of leukemia occurring in radiologists, because the notice of this patient's death gave no indication that he had been exposed to radiation. If his case were included in the radiologic group, the percentage of leukemic deaths therein would be increased to 4.3, and the percentage in the non-radiologic group, in which his case was included, would be slightly lower, thus accentuating the difference between them.

The fact that the patient was a dermatologist suggested a separate estimation of the incidence of leukemia in physicians practicing that specialty. During the ten years covered by the study, 60 physicians listed as dermatologists died. Two of them, including the one reported in this article, died of leukemia, giving a percentage of 3.3. This approaches the incidence in the radiologic group, but the number of cases is too small to be of statistical significance.

#### SUMMARY

A statistical study of 34,626 obituary notices in the *Journal of the American Medical Association*, covering the ten-year period from 1935 to 1944, reveals that the incidence of leukemia among 205 physicians listed as radiologists was 3.9 per cent, which is more than eight times as great as the incidence (0.44 per cent) among those not listed as radiologists.

This marked difference is substantial evidence that exposure to radiation is a potential cause of leukemia.

A case of lymphatic leukemia in a dermatologist who failed to take adequate precautionary measures against radiologic exposure is reported.  
99 Bay State Road

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believed that fresh vegetables, particularly the green leafy vegetables, are especially rich sources of carotene for the human dietary. In their determination of pure carotene in green vegetables, Fraps, Meinke and Kemmerer<sup>10</sup> found that green string beans contained 0.03 mg of carotene per 100 gm, beet tops 3.2 mg, sweet potatoes 4.5 to 5.7 mg, and carrots 4.5 to 8.4 mg. Zimmerman, Tressler and Maynard<sup>11</sup> report from a study of carotene in fresh and frozen vegetables that bush lima beans contain 0.24 mg per 100 gm, spinach 0.46 mg, asparagus 0.70 mg, and broccoli 1.0 mg. Unfortunately, there is likely to be a serious loss of carotene from commercial vegetables after they are harvested, particularly if they are exposed to summer temperatures in stores or on roadside stands for a considerable period of time.

Since milk is generally considered to be a rich source of riboflavin, it is interesting to compare it and the ice cream under discussion. In studies conducted on milk produced by different breeds of cows in various stages of lactation and fed a variety of rations, Snell and Strong,<sup>12</sup> Hand and Sharp,<sup>13</sup> Houston, Kon and Thompson,<sup>14</sup> Johnson, Maynard and Loosh,<sup>15</sup> Holmes, Jones, Wertz, Esselen and McKey<sup>16</sup> and other investigators found that the riboflavin content of milk varied from 0.06 to 0.34 mg per 100 gm, with an average value of less than 0.20 mg. Thus, on a weight basis, the ice cream under consideration is a richer source of riboflavin than is average milk, but ice cream is sold on a volume basis,—that is, by the pint or quart,—and because of the large amount of air that is incorporated, it contains much less riboflavin than does an equal volume of milk.

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According to Cheldelin and Williams<sup>20</sup> such common foods as beef round, pork loin, veal chop, leg of lamb, mutton shoulder, chicken leg and oysters contain about the same amount of riboflavin as was found in the ice cream under discussion, but these authors found much less riboflavin in whole-wheat bread, chicken breast, salmon, dried lima beans, cabbage and carrots, which are widely used foods. Hodson<sup>21</sup> studied the riboflavin content of about

fifty fruits and vegetables. Of these only one, broccoli, approached ice cream in riboflavin value, and only six or eight of the others contained half as much riboflavin. Thus, one may conclude from this and other studies that the ice cream under consideration compared favorably with practically all other foods as a source of riboflavin for the human dietary.

## SUMMARY

It has been estimated that the retail value of the ice cream consumed in this country annually is about one fourth that of milk and over twice that of eggs, apples or potatoes.

Samples of coffee, maple and vanilla ice cream, manufactured under plant conditions were assayed for carotene, riboflavin and ascorbic acid. The coffee, maple and vanilla ice cream contained 0.09 mg, 0.12 mg and 0.09 mg of carotene and 0.27 mg, 0.26 mg and 0.26 mg of riboflavin per 100 gm, respectively. No ascorbic acid was found, probably because of the large amount of air incorporated in commercial ice cream to increase its bulk.

Comparison of these ice creams with numerous widely used foods shows them to be excellent sources of carotene and riboflavin for the human dietary. The nutritive value of ice cream, however, varies with the nature and amount of the ingredients used and the process of manufacture.

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cream was extracted for one hour with 50 cc of acetone-sulfuric acid solution (3 parts acetone to 1 part of 1 ON sulfuric acid). After extraction acetone was added to 60 cc (the original volume), and 6.5 per cent trisodium phosphate solution was added until the reaction of the mixture was pH 4.5. Sufficient distilled water was added to make 200 cc. Fifty cubic centimeters of supernatant liquid was withdrawn, and to this there was added 7 to 10 drops of 4 per cent potassium permanganate solution and sufficient 1 per cent hydrogen peroxide to decolorize. The volume was made up to 100 cc, and the solution was filtered. Three 20-cc aliquots, designated as A, B and C, were withdrawn. One cubic centimeter of water was added to aliquot A, 1 cubic centimeter of standard riboflavin solution (0.025 mg per cubic centimeter) to aliquot B and 1 cc of water and a few crystals of sodium hydrosulphite to aliquot C. Ten cubic centimeters of each aliquot was transferred to cuvettes and read in the spectrophotometer, as described by Holmes, Jones, Wertz and Kuzmeski.<sup>4</sup>

### Reduced Ascorbic Acid

The ascorbic acid content of the ice cream was determined by a modification of the method of Holmes, Tripp, Woelffer and Satterfield.<sup>5</sup> Twenty-five grams of ice cream was weighed into a tared centrifuge tube, intimately mixed with 25 cc of a mixture of equal parts of 5 per cent metaphosphoric acid and 10 per cent acetic acid, and centrifuged for ten minutes. The mixture was filtered and repeatedly washed with 5 per cent metaphosphoric acid. Approximately 50 cc of the filtrate was transferred to a 125-cc Erlenmeyer flask, 0.5 gm of 300-mesh Bentonite was added, and the mixture was shaken vigorously for one minute, allowed to settle and filtered. Ten-cubic centimeter portions of the clear, colorless filtrate were titrated with a standard 2-6 dichlorophenolindophenol dye solution.

### RESULTS

Ten samples of coffee, of maple and of vanilla ice cream were assayed for carotene, riboflavin and reduced ascorbic acid. The results were quite uniform for all three flavors. The extreme values for carotene and riboflavin for each of the three flavors are reported below, but since close agreement was obtained for the different samples of the flavors, only the average values are reported in Table 1.

The carotene content of the coffee ice cream varied from 0.09 to 0.10 mg per 100 gm, with an average of 0.09 mg. The amount of carotene in the maple ice cream ranged from 0.11 to 0.12 mg per 100 gm, with an average of 0.12 mg. The vanilla ice cream contained from 0.09 to 0.10 mg per 100 gm, with an average of 0.09 mg. Thus, the average values for the carotene content of coffee and of

vanilla ice cream were identical, but that of maple ice cream was somewhat higher.

The riboflavin content of the ice cream was virtually uniform for each flavor. The amount in the coffee ice cream varied from 0.25 to 0.29 mg per 100 gm, with an average of 0.27 mg. The maple

TABLE 1 Vitamin Content of Ice Cream \*

EXPERIMENT No	CAROTENE	RIBOFLAVIN	REDUCED ASCORBIC ACID
	mg / 100 gm	mg / 100 gm	mg / 100 gm
1	0.10	0.27	0.00
2	0.10	0.26	0.00
3	0.11	0.26	0.00
4	0.10	0.27	0.00
5	0.10	0.28	0.00
6	0.10	0.26	0.00
7	0.11	0.26	0.00
8	0.10	0.26	0.00
9	0.10	0.25	0.00
10	0.10	0.27	0.00
Averages	0.10	0.26	0.00

\*Averages for ten samples of coffee, maple and vanilla ice cream.

ice cream contained from 0.24 to 0.28 mg per 100 gm, with an average of 0.26 mg. The amount of riboflavin in the vanilla ice cream ranged from 0.25 to 0.29 mg per 100 gm, with an average of 0.26 mg.

The reduced ascorbic acid was determined for ten samples of each of the three flavors. Only five or six of the thirty samples showed even a detectable trace of reduced ascorbic acid. These results were not unexpected, however, since, as stated above, nearly half the volume of the finished ice cream consisted of air that had been whipped into it during the freezing process. The air dispersed throughout the ice cream obviously favored rapid oxidation of the reduced ascorbic acid.

Obviously, the amount of carotene, riboflavin and reduced ascorbic acid in any ice cream is influenced by the type and amount of the materials used in its manufacture, the procedure used for preparing it and the conditions under which it is stored during the interval between manufacture and consumption. Since these factors vary widely with conditions and localities, the nutritive value of both homemade and commercial ice cream is quite variable.

### DISCUSSION

It is interesting to compare the amount of carotene found in the three flavors of ice cream — 0.09 mg, 0.12 mg and 0.09 mg per 100 gm — with that found in some other common foods. The amount in fresh whole milk is apparently quite variable, for Tuzson<sup>6</sup> found 0.003 mg per 100 gm, and Guggenheim<sup>7</sup> reported 0.028 mg, 0.017 mg and 0.010 mg per 100 gm, respectively, for milk produced in hill, valley and urban areas of Palestine. Olson, Hegsted and Peterson<sup>8</sup> state that fresh whole milk contains 0.021 mg of carotene per 100 gm, and Dornbush, Peterson and Olson<sup>9</sup> found 0.011 mg of carotene per 100 gm in March milk and 0.035 mg in September market milk. From these and other studies it is evident that the three ice creams used in this study were a much richer source of carotene than is whole milk. It is generally

believed that fresh vegetables, particularly the green leafy vegetables, are especially rich sources of carotene for the human dietary. In their determination of pure carotene in green vegetables, Fraps, Meinke and Kemmerer<sup>10</sup> found that green string beans contained 0.03 mg of carotene per 100 gm, beet tops 3.2 mg, sweet potatoes 4.5 to 5.7 mg, and carrots 4.5 to 8.4 mg. Zimmermann, Tressler and Maynard<sup>11</sup> report from a study of carotene in fresh and frozen vegetables that bush lima beans contain 0.24 mg per 100 gm, spinach 0.46 mg, asparagus 0.70 mg, and broccoli 1.0 mg. Unfortunately, there is likely to be a serious loss of carotene from commercial vegetables after they are harvested, particularly if they are exposed to summer temperatures in stores or on roadside stands for a considerable period of time.

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## CLINICAL NOTE

## SPOROTRICHOSIS\*

## REPORT OF A CASE

MAJOR SPENCER C FLO, M C, A U S, AND  
CAPTAIN PAUL E SMITH, M C, A U S

**S**POROTRICHOSIS is seldom seen in the United States and is easily confused with a number of other diseases. Strictly speaking, it presents a dermatologic problem, but the surgeon may encounter the disease in its early stages when it resembles a local infection. As it progresses and

The responsible organism is *Sporotrichum schenckii*, a fungus probably acquired in this country through contact with a plant, such as the barberry shrub, a carnation or sphagnum moss. A break in the skin seems necessary as a portal of entry, since in most of the reported cases there is a history of an open lesion while the patient was in contact with the plant. The incubation period ranges from three days to three weeks. The primary lesion appears as a deep pustule at the site of entry, which may either become chancroid in character, with induration, softening and abscess formation, or take the form of an indolent ulcer. Later the regional lymph channels become involved, causing a lymphangitis, with nodulations along the channels simulating enlarged lymph nodes, but the nodes themselves are not involved. The skin surrounding these nodules is usually reddish purple. The nodules



FIGURE 1 Photograph of the Primary Lesion

This occurred on the inner aspect of the thumb, with nodulations extending upward on forearm

lymphatic invasion occurs, it becomes evident that one is dealing with a granuloma. For this reason, one should recall the possibility of sporotrichosis when considering a skin lesion that may be due to syphilis, tuberculosis, pyoderma, coccidiomycosis, actinomycosis or tularemia.

Sporotrichosis was first described as a pathogenic entity by Schenck in 1898. Since then, about 200 cases have been reported in the United States. Five of these were from New York State, and most of the others were from the Mississippi Valley.

\*From the Surgical Service, Station Hospital, Bolling Field, D. C.

frequently break down, appearing like the original lesion. This is the most frequent form of the disease; it is described in textbooks as the "localized lymphangitic type." Constitutional symptoms are rare, and the lesions are usually painless. Some authors believe that surgery is contraindicated, but others have shown that scar formation can be greatly reduced by open drainage.

There are four other types of the disease—disseminating subcutaneous, disseminating ulcerative, epidermal and systemic. The disseminating subcutaneous type is the same as the local one except

that the lesions are scattered over the entire body without following any pathway, suggesting an invasion of the blood stream. The disseminating ulcerating type is likewise the same except for much earlier ulceration. The epidermal type involves only the skin but if these local lesions remain untreated, the deeper structures may become involved. The systemic type affects the bones, joints and muscles and is becoming more widely recognized as the causative factor in many obscure pulmonary lesions. In this phase the outlook is serious but the localized lesions readily respond to potassium iodide therapy.

The fungus is extremely difficult to find by direct smear, but Lawless suggests, as a quick method of diagnosis while awaiting the result of cultures,

to admission the lesion on the thumb had been incised. At no time had the patient felt ill or had a fever, and except for the local lesions he appeared well. On the inner aspect of the left thumb toward the flexor surface there were several deep pustules about the size of the head of a match. Around this area the skin was thin and blue (Fig 1). Along the volar surface of the forearm were many slightly tender nodules that felt like enlarged lymph nodes. There was no involvement of the axillary nodes. The temperature, pulse and respirations were normal and remained so throughout hospitalization. Urinalysis and a Wassermann test were negative. The white-cell count was 7200 with 79 per cent neutrophils, 18 per cent lymphocytes, 1 per cent mononuclear cells and 2 per cent basophils. The red-cell count was 4,750,000, and the hemoglobin 15.5 gm.

One of the pustules was opened, and a thin milky fluid exuded; a stained smear of which was negative for ordinary bacteria. Further questioning brought out the fact that 5 days before the appearance of the primary lesion the patient had been hunting rabbits, which suggested tularemia. At that time the lesions took on the characteristics of a granuloma; the nodules began to break down, and the surrounding

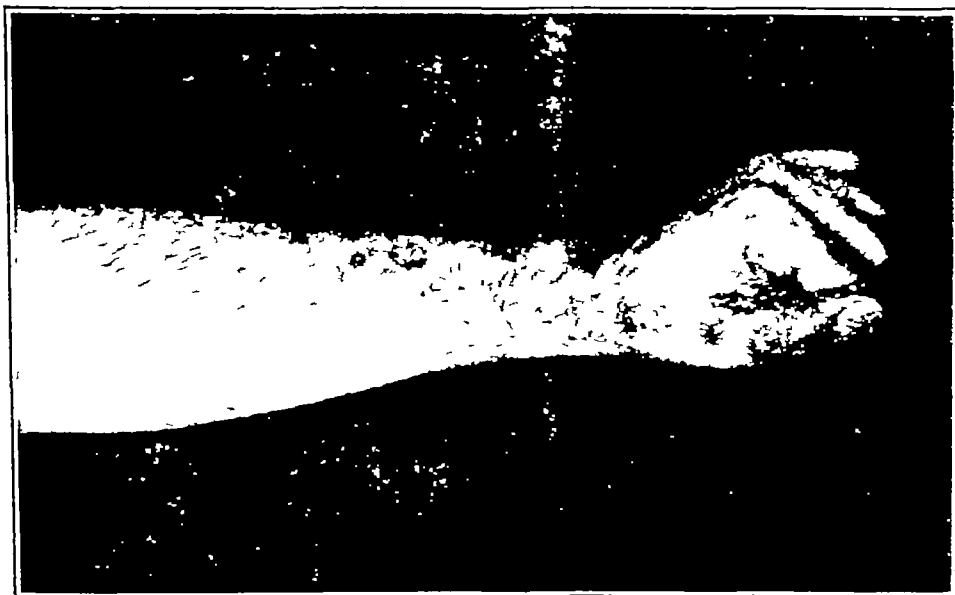


FIGURE 2 Photograph of Lesions at a Later Stage

*The nodulations ran along the volar aspect of the arm and showed characteristic ulceration and suppuration. They involved only the distal third of the forearm.*

adding a drop of Unna-Pappenheim's methyl green-pyronin stain to a drop of pus, after which the fungus can frequently be found by direct examination. Culture is the only definite method of diagnosis and is usually reliable. Pathological examination of tissue is not helpful, since the histologic picture resembles that of all the granulomas. Agglutination and cutaneous tests are of equivocal value.

#### CASE REPORT

A 41-year-old captain was admitted to the station hospital on December 2, 1944, complaining of an infection of the left thumb, with "streaks and lumps" running up the arm. He had been on a course of sulfadiazine and 100,000 units of penicillin, as well as hot compresses to the thumb. Prior

to admission the lesion on the thumb had been incised. At no time had the patient felt ill or had a fever, and except for the local lesions he appeared well. On the inner aspect of the left thumb toward the flexor surface there were several deep pustules about the size of the head of a match. Around this area the skin was thin and blue (Fig 1). Along the volar surface of the forearm were many slightly tender nodules that felt like enlarged lymph nodes. There was no involvement of the axillary nodes. The temperature, pulse and respirations were normal and remained so throughout hospitalization. Urinalysis and a Wassermann test were negative. The white-cell count was 7200 with 79 per cent neutrophils, 18 per cent lymphocytes, 1 per cent mononuclear cells and 2 per cent basophils. The red-cell count was 4,750,000, and the hemoglobin 15.5 gm.

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## SUMMARY

A case of sporotrichosis is reported, primarily for its surgical interest, since in the early stages the disease often presents itself as an ordinary infection. Early diagnosis is important, since treatment

require five to seven days before showing growth

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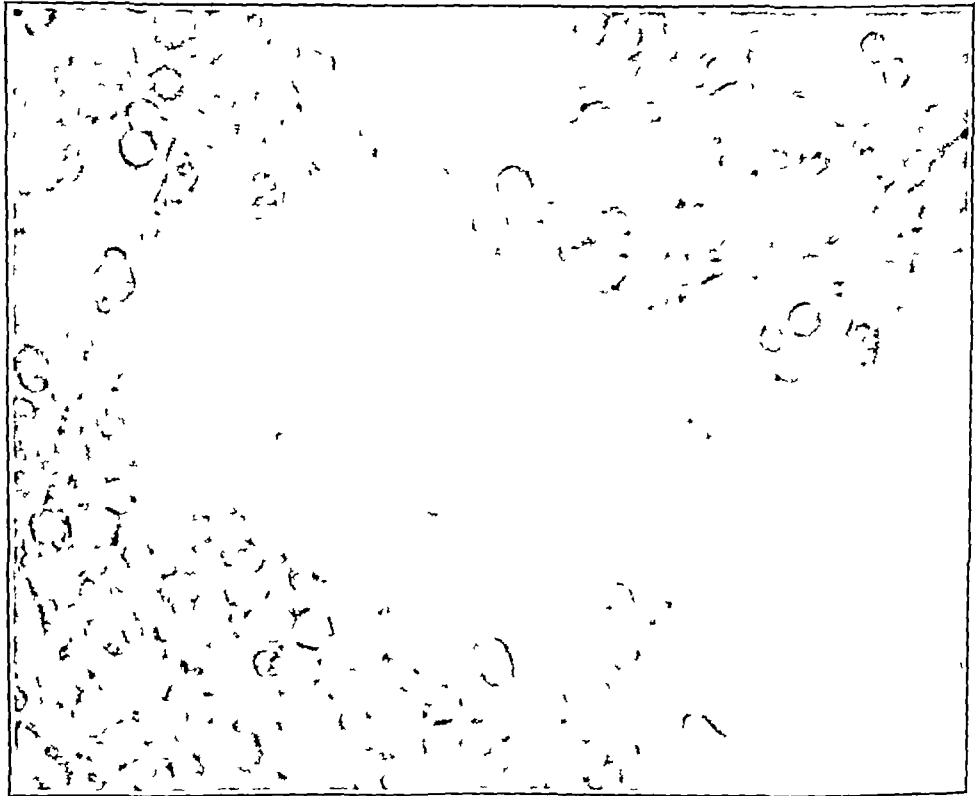


FIGURE 3 Hanging-Drop Preparation Showing Characteristic Morphology of *Sporotrichum* (high-power)

with potassium iodide is specific and prevents further advance of the disease.

The diagnosis is made through cultures, but it must be remembered that the cultures

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## SYMPOSIUM ON MEDICAL SOCIOLOGY

## PROBLEMS IN THE DISTRIBUTION OF MEDICAL CARE\*

DEAN A. CLARK, M.D.†

IT IS no accident that the Harvard Medical School has decided to hold these lectures on medical sociology. Never before has there been such widespread interest and activity in the social aspects of medicine among all groups of people — not only medical students and practicing physicians but farmers, members of labor organizations, businessmen and government officials. Ten years ago it would not have occurred to anyone to have such a lecture series, but today it seems the most natural thing imaginable.

Indeed, the question of how better to distribute medical service is constantly present. Among groups of physicians, for example, the New York Academy of Medicine has been holding a series of fifty or more weekly meetings devoted to "Medicine and the Changing Order." Then too, one can scarcely pick up an issue of a newspaper — the *New York Times*, for instance — without finding an article or perhaps an editorial dealing with the subject. Only last month a major article in *Fortune* was devoted to it, and radio forums touch on it nearly every week.

One is also reminded of the general interest in these matters by the polls of public opinion that have been appearing with increasing frequency. Although these polls differ considerably from one another in detail, all without exception show that the majority of the people believe that some change is necessary in the ways in which medical care is being distributed. A poll conducted by the American Medical Association among medical officers of the Army and Navy indicated that most of those who replied were unwilling to return to the individual practice of medicine on a fee-for-service basis.

Another constant problem is the fact that some 12,000,000 Americans now serving in the armed forces will, as veterans, have enduring rights to hospital care for both service-connected and non-service-connected disabilities for the rest of their lives, at the expense of the federal government. It is difficult to say, moreover, just what the effect will be on the millions of soldiers and sailors — and their thousands of physicians — of having received or furnished comprehensive medical service of the highest character for three years or so without the payment of any fees at all.

Besides the purely military medical services, the war has brought a number of new activities in medicine affecting civilians, and these too are bound

to affect the future of medical practice in this country. Think, for example, of the aid given to medical students by the Army and Navy. For the first time, men who wished to study medicine have been enabled through this aid to do so without regard to their financial status. Similar opportunities in nursing have been offered by the Cadet Nurse Corps. In the realm of research, the Office of Scientific Research Development, through its Committee on Medical Research, has financed an incredible amount of important scientific work in medical schools, hospitals and laboratories. The Emergency Maternal and Infant Care Program supervised by the United States Children's Bureau has paid, with federal funds granted to the states, for the care of the wives and infants of hundreds of thousands of enlisted men. It is impossible to believe that some of the benefits of these wartime activities will not be continued in one form or another after the war is over.

Other indications of the desire for improved distribution of the benefits of modern medicine are to be found in the public actions of various influential persons and groups. Less than a month ago, for example, Governor Warren, of California, stated his intention of supporting compulsory health insurance in that state. Mayor La Guardia, of New York City, has announced the initiation of a plan to provide 1,000,000 residents of that city with medical care on a prepayment group-practice basis. The American Public Health Association has recently gone on record as favoring a nationwide system of medical care for all people, supported by compulsory insurance, general taxation or a combination of the two. In another statement, some thirty physicians and laymen have urged national action to furnish complete medical care of high quality to the American people. Included in the group, incidentally, was a physician who is a recent president of the American Hospital Association and is now chairman of the Commission on Medical Care appointed by Governor Dewey, of New York. Another physician-signer of the statement has recently served two terms as president of the Massachusetts Medical Society.

Finally, of course, there are the prospects of official governmental action in this and other countries. Here there is the much discussed Wagner-Murray-Dingell Bill, in Great Britain there is the Churchill government's "White Paper" proposing a national health service, in Canada, several years of study have yielded a national health bill that includes compulsory insurance, which has been approved in principle by the Canadian Medical

\*This is the second of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January-February and March 1945. They were sponsored by the Department of Preventive Medicine and were primarily intended for third year students. These articles will temporarily replace the reports "Medical Progress."

†Senior surgeon United States Public Health Service, medical director Health Insurance Plan of Greater New York (on leave of absence).

**Association** All these proposals are sweeping in character, and they indicate the trend among important sectors of legislative opinion

So there can be little doubt that this series of lectures is indeed timely. All this interest in the better distribution of medical and health services is certainly noteworthy, but one may well ask why it has come about. Is it purely accidental that so many people are concerned about this subject, or has the feeling been aroused by a small, highly vocal minority? Or are there, perhaps, deeper reasons for it? Perhaps the title of this lecture should be changed from "Problems in the Distribution of Medical Care" to "Is There a Problem in the Distribution of Medical Care?" with the subtitle, "If So, What Is the Nature of the Problem?"

First, is there really any problem? With the lowest over-all national death rate in its history and one of the lowest in the world, should not the United States be perfectly content to let well enough alone? This is a point of view one often hears expressed. But the over-all death rate is a sweeping average and, as every science student knows, one must look behind an average to see what makes it up. Here are a few examples of disparities in death rates

In 1941, when the national death rate was 10.3 per 1000 for Whites, it was 13.7 for Negroes. In 1942, the death rate for tuberculosis for all people was 42.2 per 100,000. For Whites alone in that year it was 34, but for Negroes, it was 112, and for Indians 230. When the death rate for infants under one year of age — often considered the most accurate index of health — was 45 per 1000 live births for all people in 1941, it was only 31 in Connecticut, but in New Mexico it was 95.

It is easy to see from these examples that over-all death rates do not tell the whole story. But it may further be asked what information even the most refined figures on death rates give about people's health and their need for medical care. Obviously, figures on deaths tell practically nothing about the state of positive health, since they give no indication how many of the population are really well nourished, full of physical vigor and emotionally well adjusted. What is more, death rates do not even reveal much about the prevalence and duration of disease and disability and therefore about the need for medical care.

Indeed, a lower death rate may well be accompanied by a higher rate of disability, paradoxical as this may sound. For instance, much of the dramatic fall in the national death rate in this country has been due to control of communicable disease, especially diseases of childhood. As everyone knows, people live longer and there are proportionately more elderly persons than there used to be. The population is aging. But of course elderly persons are far more susceptible than are young ones to chronic diseases such as arthritis, cardiovascular-renal disease and diabetes, which

result in much longer disability than do most diseases of childhood. As another example, a few years ago a man might come down with an overwhelming lobar pneumonia and be dead in three days in spite of the best treatment available. Today, with the sulfonamide drugs and penicillin, such a patient might well be cured, but he would be disabled for at least thirty days — ten times the disability, ten times the need for medical and nursing care, but a live patient and a decreased death rate.

Such figures on the incidence and duration of disease and disability as exist cannot be compared with those of a generation ago, because at that time such surveys had not been made. But the examples given above at least make it clear that lowered death rates do not tell much about the state of the Nation's health and do not imply that there is less disability or less need for medical care than there was in earlier years. It seems quite probable, in fact, that the country needs more medical care than ever before, but the kind required is somewhat different. There is relatively less need in medical practice for immediate and dramatic life-saving measures, there is need for more preventive service, more care of chronic illness and more attention to the emotional, psychological and social aspects of illness. This changing pattern of medical practice is not always fully realized — or liked — by physicians, but there is no doubt that it is taking place.

It therefore seems reasonable to conclude that there is indeed a problem in the distribution of medical care. What, then, is the nature of the problem? Is it primarily a lack of adequate scientific knowledge? Obviously, this need exists and must be met, but no one can look at the present situation and not agree, also, that the knowledge now at hand is not being used effectively. The venereal diseases, for instance, can be wiped out today, but the country is still, in spite of much excellent work, a long way from this goal. So that the present problem in medicine is not simply a need for more knowledge.

Is the need principally one for more and better facilities and trained personnel? Of course this lack does exist, but in the case of physicians, for instance, once they have been released from the armed forces the Nation will not be so badly off so far as sheer numbers are concerned. The real question is whether they are available to the people who require their services. Much the same thing is true of hospital beds and trained nurses. Certainly more of them are needed, but one must also stop and ask whether the best use is being made of those now at hand. In some fields, it is true that there are absolute numerical shortages. For instance, there are not nearly enough dentists, public-health nurses, psychiatrists or medical and psychiatric social workers. Even with these groups, using what there is to the best advantage would make a

vast difference. In short, lack of facilities and trained personnel is by no means the heart of the problem.

Is the problem perhaps lack of money? The people of the United States are spending more than \$4 000,000,000 a year for health services including all funds spent by private patients, industry, charities and foundations and government agencies. To be sure, more money could be used advantageously, but many health and medical services are already being supported with great generosity. In fact, if all the funds now expended were used more systematically and distributed more equitably, the present amount would not be far short of adequate. Lack of funds is not, therefore, the entire basis of the difficulty.

If the weaknesses in the present distribution of health and medical services are not due solely to lack of scientific knowledge, facilities, trained personnel or funds, what is the real nature of the problem? There are several ways of describing it — or, it might be said, several elements in it. First, because it is perhaps the element recently most talked about, let us consider the inequitable distribution of personnel and facilities. Before the war there was one physician to 750 people in the United States, but in New York State there was one to 500 people, whereas in Mississippi there was one to 1500. Similarly with general hospital beds, there was one to 250 persons for the country as a whole, with one to 200 in New York State and one to 650 in Mississippi. And, it should be said, differences between communities within each state were as great as those between states. Even greater inequities exist in the distribution of nurses and dentists.

There can be little doubt that this uneven distribution is fundamentally the result of general economic conditions. In 1938, for example, counties with an annual per capita income of more than \$600 had eight times as many physicians relative to the population as did counties with one of less than \$100. Another factor is that physicians do not want to practice in rural areas. In 1938, even the wealthiest group of rural counties had 30 per cent fewer physicians relative to the population than did urban areas of the same per capita income. A third factor is the presence or absence of hospital and diagnostic facilities. Among counties with an annual per capita income of \$300 or less, those with no general-hospital beds had 60 per cent fewer physicians relative to the population, than did those with reasonably adequate general-hospital facilities. During the war, the inequities of distribution have grown worse. The result is that by the end of 1943 almost one third of all the counties in the United States had more than 3000 persons per physician.

The situation has been summed up in another way by Davis<sup>1</sup>

Communities of under 5000 population had 48 per cent of the population of the United States in 1929, but only 30 per cent of the physicians, and these physicians received only 18 per cent of the total gross income of all privately practicing physicians. Cities of between 5000 and 100,000 population had 23 per cent of the people and 26 per cent of the physicians, and these physicians obtained 28 per cent of the total physicians' income.

Cities of 100,000 and over had 29 per cent of the population and 44 per cent of the physicians, and these physicians received 54 per cent of the total gross income.

Another major element of the problem is the present pattern of payment for medical care. The provision of such care may be said to depend on two factors: medical need and medical demand. Medical need is composed of the actual physical and emotional requirements of a patient for a physician or for other services. This need can, of course, be determined only professionally — that is, by a physician through a medical history, a physical examination, laboratory tests and so on. But medical demand is quite another matter, and it does not necessarily correspond at all with the medical need. This demand is composed of at least three elements. The first of these is the psychologic and educational background of the patient. Is he afraid of all doctors or is he perhaps overanxious to use them? Does he know how and when to make use of available medical services? The second element is the physical presence or absence of medical personnel and facilities. There is always less demand on physicians or hospitals by patients who have to travel far to reach them than by those nearer at hand. The third element is the economic status of the patient. Can he afford to pay the physician's or hospital's bill, or is he afraid he may be unable to do so and therefore hesitant to seek medical aid? Demand is affected, too, by whether the method of payment is that of fees for service which acts in many cases as a barrier to obtaining service, or by periodic prepayment or insurance, which requires no further payment at the time of receiving service and therefore usually increases medical demand.

It is of course medical demand that largely determines the distribution of medical personnel and facilities and the receipt of medical care. It should include general social, educational and economic conditions, as well as physiological needs. These conditions are clearly beyond the power of the medical profession alone to change. The conclusion inescapably follows that the profession alone cannot appreciably alter medical demand and therefore cannot hope to influence or affect greatly the distribution of medical care. Since the latter ultimately depends on general economic and social factors, it clearly can be much altered only by general public action. The medical profession can, however, play an important role in assisting and guiding such public action into constructive and fruitful channels.



The principal facts concerning payment for and receipt of medical care today may be briefly summarized as follows. Families with incomes of less than \$1200 a year pay on the average \$43 a year per family for medical care. The same group annually receives 1900 physicians' house, office and clinic calls per 1000 persons. Forty-seven per cent of such persons receive no medical care in any one year, but this group has sixteen days of disability per capita annually. Those earning from \$2000 to \$3000 pay \$90 a year per family for medical care and receive annually 2300 physicians' calls per 1000 persons. Only 37 per cent receive no medical attention in a year, and the group has only six days of disability per person per year. The group with incomes of \$10,000 pays \$500 a year per family for medical care and receives annually 4700 physicians' calls per 1000 persons. Only 14 per cent receive no care each year, and annual days of disability are less than six per person.

It thus appeared that the lower the income group, the more days of disability and the fewer physicians' calls. The heart of the major problem is illustrated by these facts. In general, it is safe to say that, except for days of hospital care in urban centers with well developed public-hospital systems, the least care gets to the people who need it most, that is, those who have the most illnesses and the most days of disability but the least money to pay for medical care. Medical demand certainly does not follow medical need.

The problem of payment for medical care divides into two parts. First, there is what might be called "absolute inability" to pay the full cost of care, whatever the method of payment. Among families with incomes below a certain level, say \$1200 a year, the costs of medical care of reasonably good quality obviously cannot be met. Even in the prosperous year 1943, about one third of the country's population fell into this group. Persons in the lower economic levels also have larger families and more sickness than have the well-to-do. This combination of circumstances makes it totally impossible for these people to pay the full costs by themselves, even on a prepayment basis, and what they can pay must be supplemented from other sources.

It is sometimes suggested that people might be induced by educational measures to increase the amount they would be willing to spend for medical care. The proportion of family income expended for automobiles, washing machines, moving pictures, cosmetics and so forth has certainly come up sharply in recent years. Why not the same thing for health services? Possibly it could be done, but health expenditures have to compete with other human wants. Besides, people buy automobiles, lipsticks and washing machines because they *want* them — and nobody wants to have to see a doctor or a dentist.

In addition to this absolute inability to pay the full costs of medical care, there is the even more important second part of the problem of payment — namely, relative inability to pay. This affects not merely families at the bottom levels of income but those of all economic levels except perhaps the top 5 per cent. This problem arises from the fact that the incidence and severity of illness are unpredictable for the individual, yet, under the fee-for-service system, he is obliged to pay only when illness occurs. Thus, with the traditional method of payment the heaviest burden falls, in any one year, on the few persons unfortunate enough to be ill, and this burden strikes just at the time when, for the wage-earner, his income is cut off — namely, when he is ill.

For instance, 10 per cent of all the families in the population pay in a given year 41 per cent of the costs of medical care for the whole population and thirty-two per cent pay 41 per cent, so that the remaining 58 per cent pay in any one year only 18 per cent of the total cost of medical care for the country. The incidence of illness is uneven and consequently the distribution of the costs of medical care is also uneven under the fee-for-service system. Many a family with the absolute ability to pay \$150 or more a year for medical care under a planned periodic-prepayment system can suffer serious hardship or even be crushed financially by the enormous costs of a single serious illness, billed all at one time.

Two elements of the problem have so far been considered — the difficulties of the distribution of personnel and facilities and those of payment for service. But what about the organization of medical services? Medicine is no longer a one-man science; it takes diverse skills, expensive equipment and much trained assisting personnel to do a decent job today.

Now, typically, — and it is still typical, — doctors are in individual practice, with considerable duplication and waste of resources. Each has an office, the necessary equipment for x-ray examinations, metabolism tests, electrocardiograms, and laboratory procedures and an office nurse, technician or secretary. He cannot possibly use all these to their full capacity. For example, a friend of mine practicing in a Southern city is proud of his teaching appointments at two medical schools. He also has a private office, with an x-ray machine, metabolic and electrocardiographic apparatus, an adequate laboratory and an office nurse-technician-secretary. Because of his teaching and research and home and hospital calls, he is in his office only two hours a day, three days a week. All the rest of the time his fine equipment and office assistant are virtually idle.

Other evidence of poor organization in the medical services of today is found in the obvious waste of professional skill. Another friend of mine while

a resident in surgery at one of the best teaching hospitals performed one hundred and fifty major operations, most of them with little supervision. His first year in private practice, in a town where he was immediately given a hospital staff appointment and was welcomed by the profession he did only two major operations. This is obviously a serious waste. After a number of years, he may be expected to increase his work to near his capacity, but think of the wasted skill in the intervening years. Also, before he reached this point he may lose much of the technical perfection that was probably at its peak at the close of his year of residency.

Just as important a result of the present inadequate organization of medical services as its waste of resources and professional training is its failure to assure, for the benefit of the patient, the wide diversity of skills essential in good, modern medicine. The physician in individual private practice has to exercise all his ingenuity if he is to obtain for his patients — especially for the less wealthy ones — all the special services that they require. In the first place, specialists and laboratories may simply be unavailable, as in many small towns and rural areas. Even in large cities, general and special physicians and facilities are not related in an orderly manner, and the practitioner may have great difficulty in finding exactly the service that his patient needs. Second, the physician may hesitate to refer patients for consultation or laboratory tests because he knows that they will have to pay for these and it may be hard for them to do so. He may even begin to lose patients if he is too free in advising special work, he begins to get a reputation for "always sending you to a specialist," and patients hesitate to go to him for fear of the added cost. Then, too, patients who go to a specialist sometimes do not return to the original physician at all. For all these reasons, many a physician tries to handle far more than he is competent to, or he may be tempted by offers of split fees from certain specialists. In either event, the patient is the sufferer — he does not receive specialist care solely because of his medical need for it.

The lack of organization is also illustrated by competition rather than co-operation among hospitals. Take the example of four competing hospitals in a small town or in four small towns near one another — a not infrequent occurrence. Each small hospital is trying valiantly, pitifully, to do everything, and of course is unable to do so satisfactorily. A single large hospital could usually provide far better facilities and equipment than any one of the four. Yet consolidation of such rivals is all too often the exception rather than the rule. Planning of hospitals by areas or regions and by special tasks that each can be expected to perform has been strongly advocated for years,

but only recently has any serious attempt been made to carry out such plans.

There have been discussed three elements of the problem of distribution of medical care: the distribution of personnel and facilities, payment for care and organization of services. A fourth element is especially important to a group of medical students — namely, the position of the physician, and the way in which these matters affect his professional and economic opportunities.

This should first be examined from the professional outlook. Medical students are trained in every medical school and teaching hospital in this country under a system of co-operative group medical practice. They learn to apply, for the benefit of their patients, the best available technics and to use the best equipment, with the generous assistance and consultation of their ablest colleagues and teachers. Yet they usually go out into individual private practice, where they are simply unable, even with the best will in the world, to practice the kind of medicine that they learned in their training or, in many cases, to advance their professional skills while they are practicing. The practitioner is "on his own," indeed, and to be so often forces him to practice progressively poorer medicine.

*Fortune* puts it thus: "Many doctors, on going from the group practice of their internship to a largely solo method of practice, have felt that they have dropped back to a geologically older level of medicine on which they cannot hope to realize their maximum potential for service."

One may think that the professional frustration suffered by large numbers of physicians is compensated for, to a large extent, by their economic rewards, but such is not the case. It is true that few doctors starve, but fewer still get rich. All have necessarily a serious economic problem to face. To begin with, at least \$10,000 or \$12,000 has been spent on the medical education of each. The average net income of all physicians in 1929 was \$5300 a year. By 1934, the average had dropped to \$3300, and by 1941 it had come back to about \$5000. The average net income is certainly higher during the war, but in general the peacetime figures are indicative of the economic status of physicians. The average, however, does not tell the whole story in this instance either. Two thirds of physicians had incomes less than the average — which of course means that a few had extremely large incomes to bring up the average. Half of all physicians in practice were actually earning less than \$4000 net a year in 1929. This is none too much to repay the costs of medical education and to provide for a family and for retirement after sixty-five — few physicians earn much of a livelihood after that age. For every physician who had a net income of \$10,000 or over in 1929, there were two with incomes of less than \$2500.

In general, the physicians with the poorest economic status are young practitioners, general practitioners of any age and rural practitioners of any type and age. The best off are specialists in medium-sized cities who have been seventeen years in practice. It is no wonder that doctors flock into the specialties and into cities. Who would not? One cannot blame them for doing this, because they all have to try to reach a high earning power for at least a few years. The trouble is, of course, that many do not succeed. Statistically speaking, only one in eight of this class will ever have a net income of over \$10,000 a year. Naturally, each is sure that he will be the one. But it is difficult to predict.

Clearly, it is not the physician's fault that his basic economic insecurity obliges him to have a constant and intense interest in his income, to practice where money is and to keep up in the competitive race, sometimes at the expense of his professional skill and integrity. But, regardless of where the fault lies, the fact remains that physicians have a far from satisfactory economic position in the present scheme of things, and their economic position has unfortunate effects on medical practice.

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In summary, there is a problem in the distribution of medical care, the problem is not just a need for more scientific knowledge, facilities, trained personnel or money, however much some or all of these are needed. It has a number of aspects. There is inefficient and inequitable distribution of medical personnel and facilities, present methods of payment for care result in the fact that those with the greatest medical needs, such as the low-income groups, the aged and so forth receive the least care, a large section of the population could

not afford to pay the full cost of all the care they require by any method of payment, another large section cannot pay its full costs without hardship because the incidence and severity of illness are unpredictable, yet under fee-for-service payment the costs must largely be met at the time sickness occurs, there is great economic and professional waste in the present inadequate organization of medical services, the diverse skills and expensive equipment of scientific medicine are poorly integrated to give the best service to the patient, and finally, many physicians have little prospect of either professional satisfaction or economic security in the practice of medicine.

These facts present a serious challenge. There is truly a crisis in American medicine today. In the lectures to come you will hear more about these problems and about the attempts being made, here and abroad, to solve them. Certainly, the open, frank and dispassionate discussion of problems is the healthy means of reaching their solution. This you will have in this lecture series.

There is one more thing to remember. The problems of the distribution of medical and health services are not confined to the medical profession, nor can they be solved by it alone. Health is not the property of physicians but of everyone. These problems are the problems of all the people. To solve them therefore means discussion and action not only by physicians but by the medical profession as a whole, together with those in business, agriculture, labor and government, if we are to look forward with assurance to better health for the American people.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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### CASE 32021

#### PRESENTATION OF CASE

*First admission* A twenty-five-year-old man entered the hospital because albumin had been found in the urine fifteen months previously. He had had no complaints, except for occasional pain over the costovertebral angles.

Physical examination was negative.

The temperature was 98.6°F, the pulse 75, and the respirations 20. The blood pressure was 98 systolic, 78 diastolic.

The red-cell count was 4,460,000, with 80 per cent hemoglobin. The white-cell count was 7400, with 60 per cent neutrophils. The urine was cloudy, yellow and alkaline, and had a specific gravity of 1.014. It gave a ++ test for albumin; the sediment contained 3 red cells, 20 white cells and 2 epithelial cells per high-power field, and amorphous phosphates, triple phosphates and a few bacteria were seen. The nonprotein nitrogen was 20 mg per 100 cc, the serum calcium 10.4 mg, and the phosphorus 3.2 mg. A blood Hinton test was negative. An intravenous pyelogram showed a small area of calcification in the region of the middle calyx of the right kidney; the dye was excreted a little better by the left than by the right kidney. The middle calyx of the right kidney was deformed, and the area of calcification described above was included in the dye. Although both ureters were rather large, there was no definite evidence of hydronephrosis. The urinary bladder was not remarkable.

Cystoscopy showed a slightly reddened bladder. Both ureteral orifices were normal, and catheters were passed to both kidneys without difficulty. A normal flow of slightly hazy urine was obtained from each kidney. Intravenous phenolsulfonephthalein appeared in three minutes from the left kidney and in four minutes from the right. The urine from each kidney showed no cells or organisms and was sterile on culture. The patient was discharged three days after admission.

*Second admission* (five years later) During the first three years after discharge the patient had three brief episodes of severe pain in the right flank,

which radiated to the right lower quadrant. At the end of that time, several stones were removed from the bladder at another hospital. After this operation he felt well until three months before readmission, when he noticed that he tired easily. He had a sacroiliac ache on exertion, which subsided on rest. He had lost no weight. Three weeks before readmission he passed a stone by urethra.

Physical examination was negative.

The temperature was 98.6°F, the pulse 90, and the respirations 20. The blood pressure was 100 systolic, 60 diastolic.

The hemoglobin was 13.8 gm. The white-cell count was 7900. The urine was cloudy, amber and acid, with a specific gravity of 1.018. It gave a + test for albumin. The urinary sediment contained a rare red cell, 10 white cells and a rare granular cast per high-power field. Culture of the urine revealed on one occasion *Staphylococcus albus*, and on another, colon bacilli and nonhemolytic streptococci. The total phenolsulfonephthalein output was 45 per cent in two hours. The nonprotein nitrogen was 30 mg per 100 cc, the serum protein 5.5 gm, the calcium 10.4 mg, and the phosphorus 3.0 mg. The chloride was 102.1 milliequiv per liter, and the carbon dioxide combining power 26.3 milliequiv. The uric acid was 4.4 mg per 100 cc. An x-ray film of the teeth showed no evidence of apical abscesses or retained roots. An intravenous pyelogram revealed several areas of calcification scattered over both kidney shadows. Intravenous dye appeared promptly in good concentration. There was some distortion of the calyces on both sides, more marked on the left than on the right. The right calyces, pelvis and ureter were dilated, but a definite stone was not visible within the lower ureter.

The patient was discharged improved on the tenth hospital day.

*Third admission* (one year later) During the year after discharge the patient complained of intermittent, dull, burning pain over both costovertebral angles, which usually appeared in the morning following urination and lasted several hours. He passed several stones. He complained of no frequency, dysuria or bone or joint pain. The serum calcium had remained at about 10.4 mg per 100 cc, and the phosphorus at 3.0 mg. On one occasion, after ten days on a low-calcium diet, the urinary calcium output was 282 mg in twenty-four hours.

Physical examination revealed circumscribed, papular, scaly, erythematous lesions, 1 to 4 cm in diameter, on the inner aspect of the groins, the right lower leg and the forearms.

The temperature was 97°F, the pulse 90, and the respirations 25. The blood pressure was 110 systolic, 70 diastolic.

The hemoglobin was 14.9 gm. The white-cell count was 8100. The urine was light amber and acid, with a specific gravity of 1.010. It contained 3 red cells, 10 white cells and a rare hyaline cast per high-

In general, the physicians with the poorest economic status are young practitioners, general practitioners of any age and rural practitioners of any type and age. The best off are specialists in medium-sized cities who have been seventeen years in practice. It is no wonder that doctors flock into the specialties and into cities. Who would not? One cannot blame them for doing this, because they all have to try to reach a high earning power for at least a few years. The trouble is, of course, that many do not succeed. Statistically speaking, only one in eight of this class will ever have a net income of over \$10,000 a year. Naturally, each is sure that he will be the one. But it is difficult to predict.

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not afford to pay the full cost of all the care they require by any method of payment, another large section cannot pay its full costs without hardship because the incidence and severity of illness are unpredictable, yet under fee-for-service payment the costs must largely be met at the time sickness occurs, there is great economic and professional waste in the present inadequate organization of medical services, the diverse skills and expensive equipment of scientific medicine are poorly integrated to give the best service to the patient, and finally, many physicians have little prospect of either professional satisfaction or economic security in the practice of medicine.

These facts present a serious challenge. There is truly a crisis in American medicine today. In the lectures to come you will hear more about these problems and about the attempts being made, here and abroad, to solve them. Certainly, the open, frank and dispassionate discussion of problems is the healthy means of reaching their solution. This you will have in this lecture series.

There is one more thing to remember. The problems of the distribution of medical and health services are not confined to the medical profession, nor can they be solved by it alone. Health is not the property of physicians but of everyone. These problems are the problems of all the people. To solve them therefore means discussion and action not only by physicians but by the medical profession as a whole, together with those in business, agriculture, labor and government, if we are to look forward with assurance to better health for the American people.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 32021

#### PRESENTATION OF CASE

*First admission.* A twenty-five-year-old man entered the hospital because albumin had been found in the urine fifteen months previously. He had had no complaints, except for occasional pain over the costovertebral angles.

Physical examination was negative.

The temperature was 98.6°F, the pulse 75, and the respirations 20. The blood pressure was 98 systolic, 78 diastolic.

The red-cell count was 4,460,000, with 80 per cent hemoglobin. The white-cell count was 7400, with 60 per cent neutrophils. The urine was cloudy, yellow and alkaline, and had a specific gravity of 1.014. It gave a ++ test for albumin, the sediment contained 3 red cells, 20 white cells and 2 epithelial cells per high-power field, and amorphous phosphates, triple phosphates and a few bacteria were seen. The nonprotein nitrogen was 20 mg per 100 cc, the serum calcium 10.4 mg, and the phosphorus 3.2 mg. A blood Hinton test was negative. An intravenous pyelogram showed a small area of calcification in the region of the middle calyx of the right kidney, the dye was excreted a little better by the left than by the right kidney. The middle calyx of the right kidney was deformed, and the area of calcification described above was included in the dye. Although both ureters were rather large, there was no definite evidence of hydronephrosis. The urinary bladder was not remarkable.

Cystoscopy showed a slightly reddened bladder. Both ureteral orifices were normal, and catheters were passed to both kidneys without difficulty. A normal flow of slightly hazy urine was obtained from each kidney. Intravenous phenolsulfonephthalein appeared in three minutes from the left kidney and in four minutes from the right. The urine from each kidney showed no cells or organisms and was sterile on culture. The patient was discharged three days after admission.

*Second admission* (five years later). During the first three years after discharge the patient had three brief episodes of severe pain in the right flank,

which radiated to the right lower quadrant. At the end of that time, several stones were removed from the bladder at another hospital. After this operation he felt well until three months before readmission, when he noticed that he tired easily. He had a sacroiliac ache on exertion, which subsided on rest. He had lost no weight. Three weeks before readmission he passed a stone by urethra.

Physical examination was negative.

The temperature was 98.6°F, the pulse 90, and the respirations 20. The blood pressure was 100 systolic, 60 diastolic.

The hemoglobin was 13.8 gm. The white-cell count was 7900. The urine was cloudy, amber and acid, with a specific gravity of 1.018. It gave a + test for albumin. The urinary sediment contained a rare red cell, 10 white cells and a rare granular cast per high-power field. Culture of the urine revealed on one occasion *Staphylococcus albus*, and on another, colon bacilli and nonhemolytic streptococci. The total phenolsulfonephthalein output was 45 per cent in two hours. The nonprotein nitrogen was 30 mg per 100 cc, the serum protein 5.5 gm, the calcium 10.4 mg, and the phosphorus 3.0 mg. The chloride was 102.1 milliequiv per liter, and the carbon dioxide combining power 26.3 milliequiv. The uric acid was 4.4 mg per 100 cc. An x-ray film of the teeth showed no evidence of apical abscesses or retained roots. An intravenous pyelogram revealed several areas of calcification scattered over both kidney shadows. Intravenous dye appeared promptly in good concentration. There was some distortion of the calyces on both sides, more marked on the left than on the right. The right calyces, pelvis and ureter were dilated, but a definite stone was not visible within the lower ureter.

The patient was discharged improved on the tenth hospital day.

*Third admission* (one year later). During the year after discharge the patient complained of intermittent, dull, burning pain over both costovertebral angles, which usually appeared in the morning following urination and lasted several hours. He passed several stones. He complained of no frequency, dysuria or bone or joint pain. The serum calcium had remained at about 10.4 mg per 100 cc, and the phosphorus at 3.0 mg. On one occasion, after ten days on a low-calcium diet, the urinary calcium output was 282 mg in twenty-four hours.

Physical examination revealed circumscribed, papular, scaly, erythematous lesions 1 to 4 cm in diameter, on the inner aspect of the groins, the right lower leg and the forearms.

The temperature was 97°F, the pulse 90, and the respirations 25. The blood pressure was 110 systolic, 70 diastolic.

The hemoglobin was 14.9 gm. The white-cell count was 8100. The urine was light amber and acid, with a specific gravity of 1.010. It contained 3 red cells, 10 white cells and a rare hyaline cast per high-

power field. A urinary culture showed abundant colonies of *Staph albus* on one occasion and was sterile on another. A phenolsulfonephthalein test showed 47 per cent excretion in two hours. The non-protein nitrogen was 30 mg per 100 cc, the total serum protein 7.3 gm, the calcium 10.6 mg, and the phosphorus 2.7 mg. The chloride was 102 milliequiv per liter, and the phosphatase was 6.1 Bodansky units per 100 cc.

Early on the fifth hospital day the patient began to complain of generalized aches and pains, headache and an infrequent, nonproductive cough. During the day, malaise and cough continued and discomfort developed over the sternum and the left upper chest anteriorly. There was some tenderness to percussion over the left anterior chest just below the clavicle. The breath sounds were questionably diminished over this area, without dullness or rales. The abdomen was normal. An x-ray film of the chest was negative. Hemolytic streptococci were cultured from the sputum. The evidences of infection subsided in five days and the patient was discharged.

*Fourth admission* (two and a half years later). During the period after discharge the patient had had occasional episodes of cloudy urine, he had passed a stone about a year before admission. He complained of no chills, fever, hematuria or renal colic.

Physical examination was negative.

The temperature was 100°F, the pulse 90, and the respirations 20. The blood pressure was 108 systolic, 72 diastolic.

The hemoglobin was 14.3 gm. The white-cell count was 7800. The urinary sediment contained an occasional white cell and epithelial cell. The urine culture showed *Staph albus*. The urinary calcium output was 328 mg in twenty-four hours. A phenolsulphonephthalein test showed 60 per cent excretion in two hours. The nonprotein nitrogen was 31 mg per 100 cc, the total serum protein 6.2 gm, the calcium 9.4 mg, and the phosphorus 2.6 mg. The phosphatase was 4.4 Bodansky units per 100 cc, and the chloride 102 milliequiv per liter. In an x-ray film of the teeth the lamina dura was found to be preserved. A barium swallow showed that the esophagus and trachea were displaced slightly to the left in the upper neck. No definite defects were seen in the esophagus. There was no substernal displacement of the esophagus or trachea. There was a small soft-tissue thickening in the region of the thyroid gland. An intravenous pyelogram revealed many small flecky areas of calcification in the region of all the calyces of both kidneys. The bones showed slight decalcification.

The kidneys were normal in shape, size and position.

No stones were seen in the abdomen.

Stones were promptly in both kidneys.

Stones of the calyces,

calyces,

pelvis and ureter were slightly dilated. The bladder shadow was not remarkable.

An operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR JOSEPH AUB: This is an "Albrightian" case, and I am sure that I am going to be educated.

Are there any x-ray films?

DR BENJAMIN CASTLEMAN: We have films, but there is no roentgenologist to interpret them.

DR AUB: There are flecks of calcium in the kidneys, which appear to be in the calyces rather than in the parenchyma. The kidneys themselves do not look large. One can be sure that the calcium is in the calyces because the areas of calcification are obscured by the pyelogram dye. There is some slight decalcification of bone.

We have, then, a man who had been going on for many years with repeated passage of kidney stones. The kind of stones is not mentioned, although I suspect that Dr Albright knew whether they were phosphate, oxalate or uric acid stones.

DR CASTLEMAN: The record states that they showed a large amount of phosphate and a small amount of oxalate.

DR AUB: Since these were phosphate stones, it makes one think, of course, of parathyroid disease. This boy was carefully studied, however, over a long period of time and never had a high blood calcium and had only an occasional relatively low phosphorus. The high calcium output in the urine on two occasions is extremely suggestive of hyperparathyroidism and makes one think that that is the diagnosis. But that is not adequate evidence for me to make this diagnosis. I do not see the soft-tissue mass in the neck in the x-ray films, but it is said to have distorted the trachea and esophagus. But a parathyroid tumor is practically always so soft that it does not, in my experience, shift the esophagus. There is said to have been thickening around the thyroid gland, which is rather suggestive of a thyroid rather than parathyroid adenoma. In favor of hyperparathyroidism, however, are the high calcium output, the two low phosphorus determinations and the slight decalcification. This does not seem sufficient evidence to make a diagnosis of hyperparathyroidism in a patient who repeatedly had a normal blood calcium, often a normal blood phosphorus and a good lamina dura around the teeth, particularly when the disease had been going on for a long time, as judged by the renal calculi. On the contrary, it fits in better, it seems to me, with a renal condition described by Randall,\* of Philadelphia, in which calcified areas appear beneath the mucous membrane in the calyces of the kidneys and eventually break through, stones gradually accumulating around these denuded calcified areas. He found that the stones could be composed of

\*Randall, A. Initiating lesions of renal calculi. *Surg Gynec & Obst* 64: 201-208, 1937.

phosphate or oxalate or uric acid, depending on the deposition from the urine. With such a diagnosis, this patient would not be placed in the hyperparathyroid group, although I do not believe that the articles published by Randall rule out hyperparathyroidism in his cases.

I am willing to say that the surgeon who operated on this patient looked for a parathyroid tumor. I do not believe that he found it, nor do I believe that he even found large parathyroid glands, because I doubt that this man had enough renal damage to cause parathyroid hyperplasia. I think that he probably had an old pyelonephritis, which may have accentuated the production of stones.

DR EDWARD C REIFENSTEIN: I should like to give Dr Aub some blood chemical determinations that I had in my office notes but that did not get into the hospital record.

DR AUB: One set of values is as follows: calcium, 11.2 mg; phosphorus, 2.8 mg; and phosphatase, 10 Bodansky units. Another is calcium 10.9 mg and phosphorus 3.5 mg, with later a phosphatase of 5.3 units. Still another is calcium 10.3 mg, phosphorus 2.5 mg and phosphatase 5.9 units. These are suggestive of hyperparathyroidism, I admit. I think that a search for overactivity of the parathyroid glands is justified, but if I had operated on this man, I should have looked for a parathyroid tumor without conviction, and I shall end up by saying that I do not believe that they found one.

DR FULLER ALBRIGHT: If one gives a small dose of parathyroid hormone to a normal person, one may get increased calcium in the urine, although the blood calcium may still be normal. Thus, with a moderate degree of hyperparathyroidism, a patient can have a normal blood calcium and still have increased calcium in the urine and kidney stones, such a patient should have a low serum phosphorus, unless there is glomerular damage.

This case discussed by Dr Aub is one of a large group of cases that we see in the Stone Clinic in which it is difficult to rule out a mild primary hyperparathyroidism. These patients show increased calcium in the urine, a low serum phosphorus and a normal or slightly low, occasionally slightly high, serum calcium. We think that these cases are due to pyelonephritis with resulting tubular damage, as a consequence of which the kidneys lose calcium far more readily than normal ones. The sequence of events in this group can be summarized as follows: pyelonephritis, a kidney that lets calcium through more readily than normal, a tendency to a low serum calcium, secondary hyperparathyroidism to meet the tendency to a low calcium, and a low serum phosphorus. One ends up with a normal serum calcium, a low serum phosphorus, a low calcium-phosphate ion product and, hence, a tendency to osteomalacia and a high serum phosphatase, which this man had. You can see that it may be difficult to differentiate this group of cases from

those of primary hyperparathyroidism, which may have secondary urinary infection of the kidneys. As yet, we do not know any way of clinically differentiating these two groups of cases.

I do not believe that I disagree with Dr Aub in anything except that I thought that a tumor would be found. We both agree that the patient should have been operated on.

DR OLIVER COPE: In all these cases the surgeon has to have a certain sort of conviction that the patient has hyperparathyroidism, because if he is not convinced beforehand he may not go the whole length, and as you know, it is not always easy to uncover all four parathyroid glands. Obviously, uncovering three glands may not be enough under such circumstances, if the three uncovered turn out to be normal. If four glands are found with no gross evidence of disease, he must wonder if he has not overlooked a fifth, because a certain number of people have five glands. I emphasize this because the hunt often takes a long time. In other words, I believe the surgeon must be convinced that the diagnosis is correct.

I agreed with Dr Albright, as opposed to Dr Aub, that there was a good likelihood that this patient had hyperparathyroidism. So I was willing to take the time to look. The reason I say that is that I do not believe that Dr Albright has enlarged enough on some of the experiences that we have had in operating on these patients. Only a year ago we operated on just such a patient. I went away from the table very discouraged, having uncovered four parathyroid glands that, so far as I could tell, were grossly normal. I took out the largest of the four because it was a little more globular in form than the other three, and to my great delight Dr Castleman found a tiny, minute adenoma in it, and the subsequent changes of metabolism confirmed Dr Castleman's anatomic diagnosis. In other words, what one must look for is not a big adenoma but rather something about the size of the head of a black-headed pin. To go back to the x-ray findings, I paid little heed to the report of the x-ray taken after the barium swallow. If there is displacement of the esophagus or the trachea or if there is a palpable nodule in the neck, it is a thyroid, not a parathyroid, tumor. Actually I could not find anything in this case to account for the x-ray findings.

At operation we uncovered four glands. They had a disturbingly normal color. The first one, the left lower, was a little larger than the average gland but the color appeared normal, that is, the relative distribution of fat cells to epithelial parathyroid cells seemed to be within the limits of normal. That was discouraging because, if there is a hyperactive adenoma in one, the other glands ought to be atrophic. This gland did not appear to be atrophic. The upper one on the left and the two on the opposite side were then uncovered, and all were within the normal limits. I took out a portion,



about 80 per cent, of the lower one on the right because it was pear shaped, and I wanted to be sure that it did not contain a minute adenoma. I left the top of it, being quite sure that there was no adenoma in this remnant. About 20 per cent of each of the other three glands was resected, to see if Dr. Castleman could find any evidence of secondary hyperplasia.

#### CLINICAL DIAGNOSES

Parathyroid adenoma

Nephrolithiasis

#### DR. AUB'S DIAGNOSIS

Renal stones due to pyelonephritis and secondary renal calcification

#### ANATOMICAL DIAGNOSES

(Nephrolithiasis)

Normal parathyroid glands

#### PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: We sectioned all four glands and found them to be normal. In each, more than half the gland was composed of fat cells and the epithelial cells seemed to be normal in size. If this had been secondary hyperplasia or an adenoma, the fat cells would have been replaced in the case of hyperplasia by an increase in the number of cells and in the case of adenoma by an increase both in the number and in the size of the cells, in other words, hyperplasia and hypertrophy. There was no suggestion of any degree of hyperplasia or hypertrophy.

DR. AUB: Feeling much more confident, I should like to add that this work of Randall's is extremely interesting. The condition that he has described occurs in youth as well as in later life. The papillae of the kidneys develop small areas of calcification below the mucous membrane, which eventually ruptures. With the passage of urine over this denuded calcification the stage is set for the accumulation of a stone of any kind. This must be a source of a fair number of stones.

DR. CASTLEMAN: Has there been any change in the patient's condition since operation?

DR. COPE: The patient was given penicillin before and after operation to decrease the urinary infection, and he told me that after that for the first time in several years he was free of discomfort in the back bilaterally, suggesting that the infection had diminished. That is the only thing that he noticed clinically.

DR. ALBRIGHT: A culture of the urine gave no growth.

#### CASE 32022

##### PRESENTATION OF CASE

A fifty-one-year-old electrician entered the hospital complaining of chills and fever.

Eighteen months before admission, the patient drank some pasteurized but apparently spoiled milk.

A short time later he noticed chills, fever and sweating. These symptoms occurred daily and seemed worse in the middle of the day. There were occasional afebrile days, but they became less frequent. During the next two months he lost 10 pounds and became extremely weak, with a sensation of fullness in the left upper quadrant of the abdomen. He was bedridden for ten weeks. A blood culture was said to be "positive" for *Brucella abortus*. A blood transfusion resulted in marked improvement. He returned to work and felt well during the next seven months. At the end of that time he noticed enlargement of the cervical lymph nodes. He again complained of chills and fever and was hospitalized. He received a transfusion from a patient who had recovered from undulant fever and showed great improvement. Two months later he again became ill and entered a local hospital. At that time an eruption of red spots that lasted a day appeared over the entire body. A blood transfusion again improved his condition, but two months later his symptoms recurred. One month before admission he entered another hospital with chills, fever, sweating and a sensation of fullness in the left upper quadrant. At that time transfusions resulted in no improvement. He was treated with sulfadiazine. Anemia and leukopenia, which had been present since the onset of the illness, persisted. Blood cultures and agglutination tests were negative for *Br. abortus*. The blood was negative for malarial parasites.

The past history was negative.

Physical examination showed a poorly nourished, pale patient who was perspiring profusely. The mucous membranes were pale, and the tongue was smooth. Numerous fused, firm, nontender, immovable nodes were palpable on the right side of the neck, and many small, firm, discrete nodes were present in the left cervical region. The heart and lungs were normal. The spleen was firm and extended to the level of the umbilicus. The liver was percussed one fingerbreadth below the right costal margin on deep inspiration.

The temperature was 97.6°F, the pulse 80, and the respirations 20. The blood pressure was 110 systolic, 80 diastolic.

The red-cell count was 3,360,000, with 10.5 gm of hemoglobin. The white-cell count was 2600, with 63 per cent neutrophils and 28 lymphocytes. Platelets were seen in normal numbers. The urine was red and acid and had a specific gravity of 1.022. It gave a + test for albumin, and the sediment contained hyaline casts as well as 2 to 5 white cells and an occasional red cell per high-power field. The nonprotein nitrogen was 25 mg per 100 cc, and the total serum protein 4.1 gm, with 2.8 gm of albumin and 1.3 gm of globulin. The serum chloride was 97 milliequiv per liter. Tests for agglutinins against typhoid and brucellar organisms were negative. A culture of the urine showed a moderate number of

colonies of *Staphylococcus aureus* and rare diphtheroid colonies. Stool culture was negative for pathogens.

An x-ray film of the chest showed large clear lung fields. The diaphragm was somewhat low in position. The heart and upper mediastinum were not remarkable.

A lymph-node biopsy was performed.

#### DIFFERENTIAL DIAGNOSIS

**DR LOWREY DAVENPORT** We have a man of fifty-one years whose essential symptom during the period of eighteen months was recurrent fever and whose significant positive findings on physical examination were enlargement of the cervical lymph nodes, enlargement of the spleen and moderate enlargement of the liver.

In the differential diagnosis we have to consider all the possibilities that would cause a relapsing fever over a period of eighteen months, considering separately, if you will, all the possibilities causing cervical adenopathy and enlargement of the spleen, to see if we can tie in the physical findings and the symptomatology. We are faced at the onset with the gratuitous finding given in the early part of the history of a positive culture for *Br abortus*. Subsequent cultures, however, were negative, as were agglutination tests for typhoid fever and brucellosis. We have to decide what we are going to do about this one positive culture. It seems unlikely in a case that has been observed for a period of eighteen months with repeated subsequent negative cultures and agglutination tests that the finding of a single positive culture for *Br abortus* should be accepted. We are told that the patient did drink spoiled milk, but we are also told that it was pasteurized, and it is inconceivable that *Br abortus* could have been present in the milk after pasteurization. Furthermore, his clinical record over a period of eighteen months is decidedly against undulant fever: he developed a rather marked anemia, a cervical adenitis and an enlarged firm spleen, all of which are unusual in brucellosis. The course of undulant fever over a period of eighteen months should have given a better clue to the diagnosis, and in spite of the history of his having drunk spoiled milk and the one positive culture, I shall throw out that diagnosis.

In considering fevers of unknown origin lasting for this period of time, we have the more frequent types, such as hidden tuberculosis or a hidden focus of pyogenic infection, and several obscure types. Recurrent malaria appears to have been ruled out by negative smears. I believe that recurrent rheumatic fever can also be ruled out: the patient was carefully observed for eighteen months without evidence of joint involvement. When one is faced with a situation of this sort, with a hidden focus of infection, the liver is usually the cause of the prolonged fever. We are all aware that the ordinary types of pyogenic infection of long duration show

intermittent leukocytosis, and certainly after one and a half years they should give definite information concerning the site and location of the focus of sepsis. We can rule out pulmonary tuberculosis since the patient had a completely clear x-ray film, at admission, but lymph-node tuberculosis must be considered in a separate category.

In a long continued fever of this sort, with progressive anemia, we have to think of the possibility of subacute bacterial endocarditis. There was no evidence, however, of peripheral emboli, also, the blood showed a marked leukopenia rather than a leukocytosis. Furthermore, the heart was normal on physical examination. Thus, at least three of the several criteria for making the diagnosis of subacute bacterial endocarditis are lacking.

There are several rare types of prolonged fever that should be mentioned in passing. Almost by the definition of his symptoms, this man had relapsing fever. Could this have been the type of relapsing fever that is due to spirochetal organisms? I think that we can exclude this diagnosis on several grounds. It has been reported, either louse borne or tick borne, in North America, but it is an exceedingly rare condition in this part of the world. Also, it is usually, in fact almost invariably, associated with leukocytosis, and we should not expect to have the finding of enlarged cervical nodes or an enlarged spleen. So most of the common infectious types of fever can be thrown out of the picture.

We should now consider the finding of large nontender immovable cervical nodes, with an enlarged spleen, which was firm, and a moderately enlarged liver. In considering a diagnosis that ties up the enlarged cervical nodes and the enlarged spleen, two things immediately come to mind. The first and likeliest possibility on that basis is Hodgkin's disease. We are all familiar with the particular form of Hodgkin's disease that goes under the name of "Pel-Ebstein type," which is characterized by recurrent episodes of septic temperature over a period of months or years, there are lymph-node enlargement and progressive anemia, and the disease finally leads to death. This is an intriguing possibility and should be seriously considered in arriving at a presumptive diagnosis. Since we are faced with confusing laboratory data and a confusing clinical picture for one and a half years, we must take it for granted that the diagnosis that we shall make before hearing the report of the biopsy is bound to be presumptive. What is against a diagnosis of Hodgkin's disease? This man, who had been hospitalized several times in a year and a half, with repeated blood examinations, had never shown any of the characteristic changes of Hodgkin's disease in the blood picture. Although the blood findings in Hodgkin's disease are never pathognomonic, a relative leukocytosis is sometimes observed during the course of the disease and an eosinophilia is often present. We have no record here of an early

blood examination, but the meager findings we do have regarding the later blood picture seem to cast some doubt on this being the usual type of Hodgkin's lymphoma

Could these have been tuberculous cervical lymph nodes? It is possible for such nodes to cause long continued intermittent fever, although such a condition now is rare, owing to the widespread pasteurization of milk. A septic type of fever, however, accompanied by profuse sweating, and other evidence of sepsis, as described in this individual, are rare unless the nodes are involved by secondary infection. We are told that the nodes were nontender and that they showed no evidence of suppuration. So we can assume that a noncomplicated tuberculous adenitis did not cause this picture.

What other forms of blood dyscrasia can cause enlarged cervical nodes and a large spleen? This man was repeatedly observed, but apparently showed no evidence of leukemia in the peripheral blood. One must always consider the possibility of leukemia in an aleukemic phase, better termed a "sub-leukemic" phase, since the leukemic elements are present if searched for. It seems likely that sometime during the course of eighteen months the typical picture of leukemia in the peripheral blood would have been found, so that the blood dyscrasias, particularly one of the leukemias, can be discarded.

We are faced with another intriguing possibility in a patient of this sort, that is, the disseminated form of lupus erythematosus. It is a condition that has come to be recognized more and more as an entity that should be considered in the differential diagnosis of long continued obscure fevers and obscure conditions with protean manifestations. Undoubtedly, the butterfly distribution of the erythema and the erythema itself have been greatly overemphasized. We now recognize that it is possible to have hidden forms of disseminated lupus without the typical erythematous eruption and the butterfly distribution. Lupus erythematosus can cause enlargement of the cervical nodes and an enlarged spleen. Over a period of eighteen months it can produce a recurrent intermittent type of fever and a progressive anemia, and also a change in the blood picture, which in the late stages is almost invariably a leukopenia. There are other things in the history that should make us consider this diagnosis carefully. There is no report of the chronic skin change that frequently accompanies the disease, but on one hospital admission the patient had a transient erythematous rash. In the late stages of disseminated lupus, because it is a disease of protean manifestations with generalized disorder of various organs in the body, one quite frequently obtains evidence of involvement of the kidneys, such as red cells, albumin and casts, which were found in this man's urine.

How much emphasis should we lay on the reports of the urine cultures? If this man had had a focus

of infection in the kidneys sufficient to give this type of clinical course over one and a half years, I should think that the early symptoms would have been more prominent than those given in the history.

We are thus finally faced with two possibilities—Hodgkin's disease, with the Pel-Ebstein type of temperature, and the disseminated form of lupus erythematosus. We must now decide which better fits the picture. One thing is definitely against disseminated lupus. It is a disease with a predilection for young women, in certain series the incidence having been as high as 90 per cent. That does not militate completely against the diagnosis, however, because the disease has been reported in men as old as seventy. Although the chances are against lupus because of its usual sex distribution, it must be seriously considered because of the clinical course. There are two or three things against Hodgkin's disease. In the first place, the cervical nodes are described as being fixed, whereas the nodes in Hodgkin's disease, as differentiated from tuberculous nodes, are usually said to be freely movable. Also, as previously mentioned, there is no indication that during the course of eighteen months he had any of the specific changes in the blood picture that frequently accompany Hodgkin's lymphoma. The age and sex distribution, however, favor this diagnosis. It is of common occurrence in men in the third and fourth decades, whereas disseminated lupus usually occurs in the second and third decades in women. Realizing that any diagnosis is only presumptive and that a positive diagnosis can be given only by the microscopical findings, I shall put down my first choice as disseminated lupus, with Hodgkin's disease second.

DR WYMAN RICHARDSON. This patient came in while I was on service. One interesting feature was that the temperature chart showed a double peak. I do not know what that means. I might add that the description of the nodes in the record is inaccurate, they formed a real mass, which I do not believe one sees in disseminated lupus. In the cases that I have seen the enlargement has been more diffuse and not so localized. I should think that that was against disseminated lupus. I also considered the possibility of sarcoid, but I had never seen such a severe case with as high a fever. I, too, considered malaria, but the smears were negative. So I came down to a diagnosis of Hodgkin's disease, with a possibility of sarcoid.

So far as the blood picture of Hodgkin's is concerned I do not believe that one can lean on it from the negative point of view, sometimes there are suggestive features from a positive point of view. The other point I should like to make is that most patients with a big spleen have a leukopenia whatever the cause, excluding, of course, true leukemia, polycythemia and infarction of the spleen.

## CLINICAL DIAGNOSIS

Hodgkin's disease?  
Sarcoid?

## DR DAVENPORT'S DIAGNOSIS

Disseminated lupus erythematosus?  
Hodgkin's disease?

## ANATOMICAL DIAGNOSIS

Malignant lymphoma, Hodgkin's sarcoma type,  
involving cervical and retroperitoneal lymph  
nodes, spleen and bone marrow

## PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN The biopsy showed Hodgkin's disease of the sarcoma type, a very malignant form, with many Sternberg-Reed cells. The patient received x-ray treatment but died a few weeks later. At autopsy the spleen was tremendous in size, weighing over 1100 gm, and was infiltrated with yellowish nodules. Microscopically it was replaced with Hodgkin's sarcoma. There is a difference of opinion whether Hodgkin's disease is a granuloma or a neoplasm. In this laboratory we believe that it is a neoplasm rather than a granuloma, and a case like this seems to confirm our belief.

The finding of *Br abortus* in a case of Hodgkin's disease brings up the recent work of Forbus and his colleagues\*. They were able to find *Brucella* in a large percentage of cases of Hodgkin's disease.

\*Forbus W D et al. Studies on Hodgkin's disease and its relation to infection by *Brucella*. *Am J Path* 18:745-748 1942

They also injected the organisms into animals and produced a picture somewhat similar to, but certainly not characteristic of, Hodgkin's disease. This work has not been confirmed, and I believe that most pathologists are skeptical of this connection.

The abdominal and cervical nodes and the bone marrow were diffusely involved. The bone-marrow involvement might have accounted for the anemia.

DR. RICHARDSON It was not the blood picture of myelophthisic anemia.

DR. CASTLEMAN Nevertheless, the vertebral marrow was almost completely replaced by sarcoma.

DR. CHESTER M. JONES I should like to comment on the question of brucellosis. I saw a good many of Forbus's cases and talked with the group at Duke University only a few weeks ago. I think that they are in general agreement now that brucellosis has nothing to do with Hodgkin's disease. In the neighborhood of Durham brucellosis is endemic and a good many people in the community have it. Its presence in Hodgkin's disease was simply an incidental finding.

DR. CASTLEMAN Most people have thought that right along.

DR. J. H. MEANS Do we see Hodgkin's disease with tuberculosis any more?

DR. RICHARDSON We do not see it nearly so much as formerly.

DR. CASTLEMAN In the last ten or fifteen years we have seen only two or three cases of Hodgkin's disease associated with tuberculosis.

# The New England Journal of Medicine

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The Boston Medical and Surgical Journal  
Established 1828

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## NEW YORK CITY RESTRICTS THE SALE OF PENICILLIN

WHENEVER a new agent becomes available and is proved useful in the treatment of disease, a problem arises concerning the extent to which its sale and distribution should be controlled. In general, federal and local authorities have been loath to apply restrictions, and when they have made attempts to do so, they have not always succeeded in withstanding the pressure from pharmaceutical and other manufacturers who are anxious to profit from the new developments. Unfortunately, many manufacturers are always ready to cash in on any wave of popularity and are not always interested in whether or not the best public good is served by

the widespread use of the product from which they derive their profits. On the other hand, the more reputable pharmaceutical firms have learned that in the long run their own best interests coincide with those of the public welfare and are best served by the carefully controlled production and distribution of products the value of which is thoroughly proved.

There are now available federal laws and regulations governing the sale and distribution of many medicinal products. In general, the purpose of these laws is to prevent the sales in interstate commerce of new substances that may be harmful and to permit the sale of such medicinal agents only after they have been proved to be of value. The Food and Drug Administration has also attempted to control advertising and labeling so as to prevent the making of unwarranted claims, while at the same time permitting the dissemination of information concerning the proper uses of new remedies.

Since most of the known drugs and biologic agents that are therapeutically active may also produce harmful side-effects, the restrictions on the sales of such agents are readily justified. The sulfonamide drugs can readily be included in this class, and there is little doubt that serious harm may result from their uncontrolled use. Regulations for bidding over-the-counter sales of sulfonamides are readily justified on this score. The demonstration of serious sensitization from the use of these agents in ointments, bandages, cosmetics, shaving creams and similar products is sufficient reason for restricting their sales in this manner. The physician who prescribes these products implicitly assumes the responsibility for seeing that they are used in a manner that minimizes their dangerous side-effects.

In the case of penicillin, toxic reactions, although by no means absent, are relatively infrequent and usually not severe. Many manufacturers are undoubtedly most anxious to have the opportunity of including the word "penicillin" on the labels of their products and to use this as a selling point, irrespective of the amount, activity or usefulness of the material that is incorporated. Great pressure will probably be brought to bear, as soon as the antibiotic is produced at a sufficiently low cost, to obtain permission to include penicillin in oint-

ments, bandages, eye lotions, shaving creams and many other products in which the particular manufacturers are interested. That such practices are not in the public interest is readily apparent to physicians, but it remains to be seen whether it is possible legally to prevent them. The facts that the manufacture of penicillin is largely in the hands of large and reputable manufacturers and that each batch must be carefully tested and approved by the Food and Drug Administration, may serve as a deterrent. Unscrupulous manufacturers, however, are not likely to submit to such rigid control, since the increased cost would make their ventures less profitable.

The Department of Health of the City of New York\* has recently added a section to its Sanitary Code that re-

stricts the sale of preparations containing penicillin or other antibiotic drugs to persons presenting a written prescription of a physician, dentist, podiatrist or veterinarian, except in the case of preparations that the Department of Health may specifically exempt from the provisions of that section. This action was based on the fact that indiscriminate use of penicillin and other antibiotics may be dangerous. One of the hazards listed is that undertreatment in many diseases may alleviate the symptoms of illness without curing the disease, which, in turn, may continue to produce damage in the patient and to be communicable to other persons. Other reasons given were that "there is accumulating evidence of the possible importance of the development of penicillin-fast strains in persons who are inadequately treated" and that "antibiotic drugs have been so recently developed that there has not been sufficient time to determine the possible toxic reactions." Whenever evidence

is presented to the Department of Health that a certain preparation containing an antibiotic is entirely harmless yet effective in the treatment of disease, the matter of exemptions is duly considered. Under this provision an exception has already been made that permits the over-the-counter sale of bandages that contain a specified concentration of tyrothricin for external application to the human skin.

The action of the health authorities of New York City is certainly a step in the right direction. The principles on which this step was based are particularly commendable. It is doubtful that many other local authorities would have been willing to apply those principles to the dispensing of penicillin, on the other hand it is hoped that this regulation will lead to similar steps elsewhere.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to.

George L. Schadt, *Chairman*  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

### ROUTINE BLOOD TESTS FOR SYPHILIS

THE value of routine blood tests for syphilis in large groups of people has been demonstrated again and again as an essential item in control of the disease. If further evidence is needed, a recent analysis of 5000 inductees in whom positive serologic tests for or a definite history of syphilis were found is convincing †

In nearly 60 per cent of the group syphilis had not been recognized and consequently had not been previously treated. At the same time it is pointed out that more evidence than a single positive serologic test is necessary to establish a diagnosis of syphilis. Thus, in 11 per cent of the cases no diagnosis of syphilis could be made after a careful history, detailed physical examination, spinal-fluid examination and further blood examinations. In another 11 per cent the syphilis had apparently

\*Sale of antibiotic drugs restricted. *Quart. Bull. Dept. of Health, City of New York* 13:33 1945

†Zellermayer, J. Syphilis in inductees: analysis of 5000 cases. *J. Fen. Dis. Inform.* 25:194-198, 1945

been adequately treated, since no evidence of the disease was found. In 13 per cent, the disease had progressed to a point where cerebrospinal, cardiovascular or other complications were demonstrable. In the remainder (65 per cent) the disease had been inadequately treated or untreated, and although evidence of disease still persisted, there were no complications. The last group contained a few cases of primary and secondary syphilis, but the bulk of them were early latent cases, with a few late latent cases, in other words, the disease was recognized before any of the serious organic changes had appeared.

The report emphasizes the need of careful diagnostic work to avoid the treatment of nonsyphilitic persons. The positive serologic test is a pointer toward the diagnosis of syphilis, but too much reliance should not be placed on the result of a single test and the patient's history should be obtained and his examination should be conducted with proper care.

## MASSACHUSETTS MEDICAL SOCIETY

### BLUE TRIANGLE EXPANDS

Since the inauguration of the Blue Triangle late in 1944 much progress has resulted in making this plan available on both a statewide and a nationwide basis. The Massachusetts Medical Society, the Massachusetts Dental Society and the Massachusetts Bankers Association have co-operatively produced and promoted the Blue Triangle to the extent that this service is now available in forty-five Massachusetts banks. In one bank alone it is reported that more than sixty of their local physicians and dentists are now using this modern method to assist their patients in paying for essential medical and dental care.

Inquiries about the Blue Triangle have been received from various sources in forty-five of the forty-eight states. This is most encouraging, for once again Massachusetts has led the way with a splendid example of co-operation directed to the public welfare.

The medical profession has already developed the Blue Cross—a prepayment plan for hospitalization—and the Blue Shield—a prepayment plan for medical care. Both plans are like insurance—fine if there is a loss and if the particular loss is fully covered. But certain people are not so insured,

or their particular expenses are not covered. The Blue Triangle fills this need.

For the benefit of those doctors who have just returned from the service and may not be acquainted with the Blue Triangle, and for those who may have overlooked investigating its possibilities, the following is a brief outline of how the plan operates. When the patient contracts for or has accrued a bill larger than he can ordinarily pay out of a week's or month's wages, he is asked by the physician if he would prefer to pay the sum due in regular installments over a six-month to twelve-month period at the local bank that is participating in the plan. If the patient agrees, he signs a note, which the doctor transfers to the bank. The patient then repays the bank in monthly installments. In this way the doctor receives his money from the bank at the time he sends them the note, less a reserve (ordinarily 10 per cent). This reserve is paid to the doctor on final payment of the note by the patient. In this way the patient obtains a loan when he needs it with a minimum of effort and at a rate lower than he could obtain on a regular personal loan.

The Blue Triangle, although it has made great strides in the past year, is expected to be of even greater service in the years to come. With so many men and women coming out of the service who will again be calling on the family doctor, the Blue Triangle is bound to be of use to them when unexpected medical expenses arise. This is especially true when people are able to buy automobiles, appliances and the many other things they are waiting for. Furthermore, returning doctors who are re-establishing their practices will find it helpful from a financial standpoint.

The Blue Triangle is truly a health-financing service. Additional information regarding the plan may be obtained from the Massachusetts Medical Society.

### DEATHS

DAVENPORT—Benita C Davenport, M D, of Middleton, died December 20. She was in her fifty-eighth year.

Dr Davenport received her degree from the Boston University School of Medicine in 1930. She became assistant physician at Essex Sanatorium in 1933 and served as senior physician from 1937 until ill health forced her to retire in 1943. She was a fellow of the American Medical Association and a member of the American Tuberculosis Association, the American Sanatorium Association and the American Trudeau Society.

Two sisters survive.

DRUMMEY—Nicholas D Drummey, M D, of Dorchester, died December 18. He was in his eighty-first year.

Dr Drummey received his degree from Harvard Medical School in 1887. He was the oldest alumnus of the Carney Hospital and was a consultant on the staff of the Faulkner Hospital. He was a fellow of the American Medical Association.

A son survives.

MASSACHUSETTS DEPARTMENT  
OF PUBLIC HEALTH  
COMMUNICABLE DISEASES IN  
MASSACHUSETTS FOR NOVEMBER, 1945

RÉSUMÉ

DISEASES	NOVEMBER 1945	NOVEMBER 1944	SEVEN YEAR MEDIAN
Anterior poliomyelitis	50	35	7
Chancroid	1	2	*
Chicken pox	771	1025	1025
Diphtheria	18	28	21
Dog bite	644	590	592
Dysentery bacillary	9	24	24
German measles	55	55	55
Gonorrhea	509	445	421
Granuloma inguinale	0	1	*
Lymphogranuloma venereum	1	2	*
Malaria	41	50	2
Measles	657	353	816
Meningitis meningococcal	10	28	12
Meningitis Pfeiffer bacillus	3	5	2
Meningitis pneumococcal	3	2	3†
Meningitis staphylococcal	0	1	0†
Meningitis streptococcal	0	0	0†
Meningitis other forms	4	3	2†
Meningitis undetermined	2	4	4†
Mumps	523	914	399
Pneumonia lobar	92	162	233
Salmonella infections	7	4	5
Scarlet fever	466	776	704
Syphilis	391	420	420
Tuberculosis pulmonary	273	217	215
Tuberculosis other forms	9	11	17
Typhoid fever	3	1	2
Undulant fever	5	4	5
Whooping cough	659	498	557

\*Made reportable December 1943

†Four-year average.

COMMENT

Cases of lobar pneumonia were reported less frequently during November, October and September than at any time during these same months since 1918, they were about one third the seven-year median

The number of cases of scarlet fever during November was substantially below the seven-year median and approximately 30 per cent less than that during November, 1944

Whooping cough remains higher this year than for comparable periods last year

Cases of anterior poliomyelitis dropped from 136 in October to 50 in November The latter figure, however, represents the highest number of cases for November since 1935, when 58 cases were reported

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Becket, 1, Boston, 7, Brockton, 1, Brookline, 1, Chelsea, 1, Chicopee, 1, Everett, 1, Fitchburg, 5, Groton, 1, Haverhill, 1, Lowell, 1, Lynn, 2, Malden, 2, Marlboro 1, Medford, 1, Orleans, 1, Palmer, 1, Pepperell, 1, Pittsfield, 1, Princeton, 1, Quincy, 3, Reading, 2, Saugus, 1, Somerville, 1, Walpole, 2, Wareham, 2, Watertown, 1, Weymouth, 4, Worcester, 2, total, 50

Diphtheria was reported from Adams, 1, Boston 6, Gloucester, 4, Lowell, 1, Malden, 1, Melrose, 1, New Bedford, 1, Somerville, 2, Winthrop, 1, total, 18

Dysentery, amebic, was reported from Boston, 1, total, 1

Dysentery, bacillary, was reported from Boston, 2, Braintree, 1, Cambridge, 2, Camp Edwards, 1, Lowell, 2, Malden, 1, total, 9

Encephalitis, infectious, was reported from Lawrence, 1, Worcester, 1, total, 2

Lymphocytic choriomeningitis was reported from Quincy, 1, total, 1

Malaria was reported from Boston, 8, Brookline, 1, Camp Edwards, 5, Cambridge, 2, Cushing General Hospital, 2, Dedham, 2, Everett, 2, Gloucester, 1, Lunenburg, 1, Lynn, 1, Fort Devens, 8, Milton, 1, Regional Hospital (Waltham), 5, Springfield, 1, Wakefield, 1, total, 41

Meningitis, meningococcal, was reported from Auburn, 1, Boston, 3, Fall River, 1, Framingham, 1, Marblehead, 1, North Adams, 1, Quincy, 1, Topsfield, 1, total, 10

Meningitis, Pfeiffer-bacillus, was reported from Cambridge, 1, Mansfield, 1, Randolph, 1, total, 3

Meningitis, pneumococcal, was reported from Brookline, 1, Natick, 1, Swampscott, 1, total, 3

Meningitis, other forms, was reported from Boston, 3, Milton, 1, total 4

Meningitis, undetermined, was reported from Haverhill, 1, Worcester, 1, total, 2

Salmonella infections were reported from Boston, 1, Billerica, 1, Brookline, 1, Lowell, 1, Malden, 2, Salem, 1, total, 7

Septic sore throat was reported from Boston, 1, Fall River, 1, Lynn, 1, Newbury, 1, Somerville, 1, total, 5

Tetanus was reported from Boston, 1, Framingham, 1, total, 2

Trichinosis was reported from Boston, 2, total, 2

Typhoid fever was reported from Boston, 1, Lawrence, 1, Waltham, 1, total, 3

Undulant fever was reported from Brookline, 1, Taunton, 2, Waltham, 1, Worcester, 1, total, 5

MISCELLANY

DR DENNY RETIRES

Dr Francis P Denny retired in November of this year as health officer of Brookline, after thirty-two years of unique service to that community Born in 1869, Dr Denny graduated from Harvard College in 1891 and from Harvard Medical School in 1895 He served an internship at the Massachusetts General Hospital, studied a year and a half in Berlin and Vienna and established himself in practice in Brookline in 1897

Among his contributions to public health were the establishment of a bacteriologic laboratory in Brookline in 1899, — the first in Massachusetts outside Boston, — the establishment of a tuberculosis pavilion as part of the Brookline Contagious Hospital in 1914 and the establishment of a dental dispensary in 1915 He inaugurated immunization against diphtheria in Brookline in 1923

For twenty-six years Dr Denny was responsible for the quarterly publication of the *Brookline Health Bulletin*, a sheet that is delivered to every household in the town, printing regularly the results of milk examinations, the rating of restaurants and much other timely health advice During his term of office Brookline was three times the winner of the health-conservation contest sponsored by the United States Chamber of Commerce

Dr Denny, in the course of a long and useful career, has been president of the Massachusetts Public Health Association, the Norfolk District Medical Society and the Brookline Anti-Tuberculosis Society and a member of the Executive Committee of the Massachusetts Tuberculosis League, now being its honorary vice-president

He has been succeeded as health officer by Dr Alfred L Frechette, a graduate of the University of Vermont Medical School in 1934 and of the Harvard School of Public Health in 1939 Dr Frechette was with the United States Public Health Service in North Africa in 1943 and 1944 and has been personal representative of Director Herbert H Lehman, of the United Nations Relief and Rehabilitation Administration, in Ethiopia He has been secretary of the New Hampshire State Board of Health for the past two years

LIST OF POTENTIALLY DANGEROUS  
MATERIALS USED IN INDUSTRY

The following list of potentially dangerous materials used in industry has been recently prepared by the Division of Occupational Hygiene, Massachusetts Department of Labor and Industry The italicized items are trade names

MATERIAL	COMPOSITION
Acetylene tetrachloride	Tetrachlorethane
Agate	Chiefly free silica
Aqua ammonia	Ammonium hydroxide (ammonia water)
Aqua fortis	Nitric acid
Aqua regia	Nitric and hydrochloric acids
<i>Arcklor</i>	Chlorinated diphenyl
Banana oil	Amyl acetate
<i>Barco spot remover</i>	Benzol (25%) and carbon tetrachloride (75%)
<i>Betastol</i>	Petroleum naphtha
<i>Blacolor</i>	Trichlorethylene
<i>Carrene</i>	Methylene dichloride
Caustic soda	Sodium hydroxide
<i>Cecolene</i>	Trichlorethylene
<i>Celiste</i>	Diatomaceous earth (silica)
<i>Ceresan</i>	Contains ethyl mercury phosphate
Chalcedony	Chiefly free silica
Chert	Chiefly free silica
<i>Chlorox</i>	Dichlorethyl ether
<i>Chlorox</i>	Sodium hypochloride



MATERIAL	COMPOSITION
Chrome green	Contains lead chromate
Chrome yellow	Lead chromate
Chrysotalsite	Free silica
Circosol	Trichlorethylene
Coal gas	Carbon monoxide
Coal tar naphtha	Contains xylene
DDT	Dichlor diphenyl trichlorethane
Diatomaceous earth	Chiefly free silica
Ditto (duplicating ink)	Methyl alcohol (90%)
Dowcylene	Carbon tetrachloride
Dowicide	Chlorophenols
Dykanol	Chlorinated diphenyl
Fibrocel	Free silica and asbestos
Filter aid	Free silica
Flake caustic	Sodium hydroxide
Flint	Free silica
Freon 12	Dichlor difluoromethane
Fusel oil	Mostly amyl alcohols
Granite	Free silica (33%)
Gunk	Emulsifying agent in kerosene, with cresol (3-4%)
Halowax	Chlorinated naphthalene
Handyflux	Contains potassium fluoride
Hexone	Methyl isobutyl ketone
Kieselguhr	Chiefly free silica
Larox	Sodium fluorosilicate
Litharge	Lead oxide
Lye	Potassium or sodium hydroxide
Mersol	Denatured alcohol, ethyl acetate and gasoline
Methyl acetone	Methanol, methyl acetate and acetone
Muriatic acid	Hydrochloric acid
Nescol	Benzol (60%)
Oil of vitriol	Sulfuric acid
Pear oil	Amyl acetate
Perchloroethylene	Tetrachlorethylene
Per-cylene	Tetrachlorethylene
Permacolor	Trichlorethylene
Petrobenzol	Petroleum naphtha
Philloto	Ether trichlorethylene or tetrachlorethylene
Prussic acid	Hydrogen cyanide
Pyranol	Contains chlorodiphenyl
Pyrene	Carbon tetrachloride
Quartz	Free silica
Quartzite	Free silica
Sand	Chiefly free silica
Santocel	Free silica
Silica gel	Free silica
Skellysol	Petroleum naphtha
Soda ash	Sodium carbonate
Solox	Denatured alcohol, ethyl acetate and aviation gasoline
Solvento	Toluol, xylol and naphtha
Sosanol 5	Naphtha
Sosanol 73	Petroleum naphtha (41%), benzol (4%) and toluene (55%)
Sosanol 74	Petroleum naphtha (15%) and xylol (85%)
Stoddard solvent	High boiling naphtha
Sirippet (paint remover)	May or may not contain benzol
Synasol	Denatured alcohol (formula 1), ethyl acetate and aviation gasoline
Taxite (paint remover)	Benzol (30%)
Tollac	Benzol (50%)
Triad	Trichlorethylene
Triasol	Trichlorethylene
Triclene	Trichlorethylene
Triclin	Trichlorethylene
Tripoli	Chiefly free silica
Troluol	Petroleum naphtha
Tromex	Trichlorethylene
V M and P naphtha	Petroleum naphtha
Varol	High boiling naphtha
Wood alcohol	Methanol

## BOOKS RECEIVED

The receipt of the following books is acknowledged and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Trauma in Internal Diseases With consideration of experimental pathology and medicolegal aspects* By Rudolf A. Stern, M.D., assistant attending physician, City Hospital, New York City. With a foreword by Francis C. Wood, M.D., director of laboratories and of the Radiotherapy Department, St. Luke's Hospital, New York. 8° cloth, 575 pp. New York: Grune and Stratton, 1945. \$6.75.

The author has endeavored to present a series of critical case histories, especially those with exhaustive post-mortem findings, along with a description of experimental work, which has either confirmed or refuted the assumption of trauma as an etiologic factor for many internal diseases. In writing the text, the author has reviewed a great mass of literature represented in a bibliography of forty-three pages, which will be found at the end of the book. The material covers the whole range of internal diseases.

*New Steps in Public Health Twenty-second annual conference of the Milbank Memorial Fund, April 12-13, 1944* 8°, paper, 148 pp., with figures and tables. New York: Milbank Memorial Fund, 1945.

This second volume of the 1944 conference is devoted to a discussion of chronic disease, medical care and the role of emotional and social factors in illness and to a number of articles on the public-health aspects of nutrition, written by various persons.

*On Modern Syphilotherapy, with Particular Reference to Salvarsan* By Albert Neisser, M.D. Translated by Isabelle von Sazenhofen Wartenberg. With a biography and bibliography by Frances T. Gardner. 4°, cloth, 42 pp., with frontispiece. Baltimore: Johns Hopkins Press, 1945. \$1.00.

In this translation Miss Wartenberg has made available the paper of Dr. Neisser, first published in 1911. The text of the article is preceded by a short biography of the author, and appended to the text there is a complete bibliography of the writings of Dr. Neisser from 1874 to 1916. The volume is well bound and is a reprint from the *Bulletin of the History of Medicine*.

## NOTICES

### ANNOUNCEMENTS

Dr. James A. Halsted and Dr. Stanley Kimball announce the reopening of their offices with the Dedham Medical Associates at 743 High Street, Dedham. Dr. Curtis Prout will be associated with them.

Dr. Francis X. Walsh, having returned from active service with the United States Army, announces the reopening of his office at 632 Columbia Road, Dorchester.

### NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, January 16, at 8 p.m. Dr. Arthur L. Watkins will speak on the subject "Studies in Electro-Diagnosis as Applied to Peripheral Nerve Injuries and Poliomyelitis."

A council meeting will be held at 6:00 p.m., followed by a dinner in the Empire Room at 6:30 p.m.

Members of the medical profession are cordially invited to attend the meeting.

### PHI DELTA EPSILON SOCIETY

A meeting of the Phi Delta Epsilon Society will be held in the auditorium of Boston University School of Medicine, on Thursday, January 17, at 8:15 p.m. Dr. Samuel A. Levine will speak on the subject "Cardiac Murmurs." Those interested are invited.

### SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JANUARY 17

FRIDAY, JANUARY 18

- \*9:00-10:00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.
- \*9:00-10:00 a.m. War and Nerves. Major Merrill Moore, U.S.A. Joseph H. Pratt Diagnostic Hospital.
- \*10:00 a.m.-12:00 p.m. Medical staff rounds. Peter Beat Brigham Hospital.
- 10:50 a.m. Industrial Dermatoses. Dr. John G. Downing. (Post graduate clinic in dermatology and syphilology.) Amphitheater, Dowling Building. Boston City Hospital.

MONDAY, JANUARY 21

- \*12:00 m.-1:00 p.m. Clinicopathological conference. Peter Beat Brigham Hospital.

TUESDAY, JANUARY 22

- \*9:00-10:00 a.m. Medical clinic. Infants Hospital.
- \*12:15-1:15 p.m. Clinicorontogenological conference. Peter Beat Brigham Hospital.

WEDNESDAY, JANUARY 23

- \*9:00-10:00 a.m. Surgical Aspects of Gastric and Duodenal Ulcer. Dr. Edward A. Cooney. Joseph H. Pratt Diagnostic Hospital.
- \*12:00 m. Clinicopathological conference. Children's Hospital.
- \*7:15 p.m. Graduate seminar in pediatrics. Children's Medical Service, Amphitheater 3A. Massachusetts General Hospital.

\*Open to the medical profession.

(Notices continued on page xvi)

# The New England Journal of Medicine

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## PROGRESS IN THE TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS\*

CUTTING B FAVOUR, M D,† CHARLES A JANEWAY, M D,‡ JOHN G GIBSON, II, M D,§  
AND SAMUEL A LEVINE, M D||

BOSTON

IT IS extremely gratifying for the medical profession to witness progress in therapy, especially when it applies to ailments that were formerly fatal. To the diseases of this kind, such as diabetes, pernicious anemia, Addison's disease and various forms of bacterial meningitis, which in the past almost always resulted in death it may soon be possible to add some types of bacterial endocarditis. Among the common diseases of the heart, none has been so resistant to treatment and so invariably fatal as subacute bacterial endocarditis. Although isolated cures occurred before the introduction of the sulfonamides, there is little evidence that any previous type of therapy materially influenced the outcome. The purpose of this paper is to summarize briefly the experience of the Peter Bent Brigham Hospital in the treatment of 347 cases of this disease during the years 1913 through 1944.

The thirty years covered by this study have been divided into three periods. During the first period, 1913-1937, termed "the pre-sulfonamide era," a great many therapeutic procedures were carried out. During the second period, 1937-1944, called "the sulfonamide era," various sulfonamides were employed¶, and during the last period, from January, 1944, to the present writing, termed "the penicillin era," penicillin has been used\*\* In the first period, 237 cases of subacute bacterial endocarditis were observed, during the second 90 cases, and during the third 20 cases.

### PRE-SULFONAMIDE ERA

The extraordinary fact stands out that before the introduction of sulfonamide therapy there was not

\*From the Department of Medicine, Harvard Medical School, and the Medical Clinic, Peter Bent Brigham Hospital.

†Associate in medicine, Peter Bent Brigham Hospital, instructor in medicine, Harvard Medical School.

‡Senior associate in medicine, Peter Bent Brigham Hospital, assistant professor of pediatrics and instructor in bacteriology and immunology, Harvard Medical School.

§Associate in medicine, Peter Bent Brigham Hospital, instructor in medicine, Harvard Medical School.

||Physician, Peter Bent Brigham Hospital, assistant professor of medicine, Harvard Medical School.

¶In this period 5 patients with patent ductus arteriosus and bacterial endocarditis also received a sulfonamide but these were operated on and are therefore not included in this series.

\*\*In this period, 1 patient with patent ductus arteriosus and bacterial endocarditis received penicillin, but was operated on and is not included in this series.

a single known recovery in this series. Of the 237 patients treated in this period, 218 died in the hospital or shortly after discharge, and the rest went home critically sick and were not heard from. Among other hospital patients a temporary cure or arrest may have occurred, since there were several cases of apparent recovery in patients with a mild-course who had some of the evidences of subacute bacterial endocarditis but failed to show a positive blood culture. These cases were not included in the study.

It is interesting and somewhat humiliating to recall the variety of bizarre and fanciful methods of treatment that were tried in pre-sulfonamide days. One patient was infected with ratbite fever (*Spirillum minus*), another was given malaria, and a third was treated with typhoid vaccine shortly after fever therapy was introduced in the treatment of general paresis. A fourth patient received intramuscular turpentine to produce a sterile abscess, a fifth received intravenous bacteriophage, and a sixth had a resection of the breast with searing of the pectoral muscle, which had been advised by Bier<sup>1</sup>. Others were given antistreptococcus goat serum or various chemicals, such as neosalvarsan, Optochin, gentian violet and acriflavine. Finally, in 2 cases living beta-hemolytic streptococci in increasing doses were injected subcutaneously with the hope of altering the immune state of the host. In no case was the outcome altered.

### SULFONAMIDE ERA

Of the 90 cases in the second period, 55 received adequate treatment with one or another of the sulfonamide drugs, and 35 either were not diagnosed soon enough or received inadequate chemotherapy. The patients who received a satisfactory course of a sulfonamide can be further subdivided into two groups. Thirty-nine received the drug alone, and 16 were given fever therapy in conjunction with it.

Among the 39 patients who received a sulfonamide without fever therapy, there were no recoveries. Courses of sulfanilamide, sulfapyridine, sulfathiazole and sulfadiazine, alone or in sequence, were

used In 2 of these cases continuous intravenous heparin was given in conjunction with oral sulfapyridine, and in 1 dicoumarin was given with sulfadiazine. Heparin therapy was discontinued because of its apparent ineffectiveness, its cost and the difficulty of administration, and finally because of a fatal cerebral hemorrhage, probably due to em-

with the sulfonamides was their combination with fever therapy. Although great interest in the use of artificially induced fever in the therapy of bacterial disease followed the meeting of the Fever Conference in 1935,<sup>4</sup> the emphasis in treatment remained on the diseases in which the in vitro sensitivity of the infecting organism to elevated

TABLE 1 Summary of Data \*

CASE No	AGE	SEX	PROBABLE DURATION OF INFECTION	DENTAL HISTORY	SPECIES INFECTING ORGANISM	PENICILLIN SENSITIVITY	APPROXIMATE TREATMENT	RESULT	FOLLOW-UP
						units/cc			
1	14	F	1 mo	Infected tooth†	<i>Str viridans</i>	—	Sulfapyridine, 1 gm every 4 hr for 11 days; sulfathiazole, 1 gm every 4 hr, with 11 infra-red treatments	Well	4 yr
2	25	M	19 days		<i>Str viridans</i>	—	Sulfadiazine, 1 gm every 4 hr, with 15 typhoid chills	Well	2 yr
3	25	M	2 mo	Gum infection	<i>Str viridans</i>	—	Sulfathiazole, 1 gm every 4 hr; sulfadiazine, 1.5 gm every 4 hr, with 10 typhoid chills	Well	3 yr
4	30	F	3 mo		<i>Str viridans</i>	—	Sulfadiazine, 1 gm every 4 hr, with 9 typhoid chills	Well	2 yr
5	20	F	1 mo		<i>Staph albus</i>	0.600-0.015	Penicillin 100,000 units a day by constant intravenous drip for 10 days and 8300 units intramuscularly every 3 hr for 9 days; Sulfadiazine 1 gm thrice daily, maintenance dose; Penicillin 300,000 units a day by constant intravenous drip for 11 days and 50,000 units every 2 hr intramuscularly for 10 days	Relapsed in 6 wk	
								Relapsed in 2 mo and died from another cause 10 mo later	
6	52	F	3 mo		<i>Str viridans</i>	—	Sulfadiazine 1 gm every 4 hr with 5 typhoid chills; sulfadiazine, 1 gm every 4 hr and neoraphenamine, 400 mg, with 7 typhoid chills; Penicillin 240,000 units a day by constant intravenous drip for 12 days	Well, subsequent heart failure	1 yr
7	38	M	10 wk		<i>Str viridans</i>	—	Penicillin 240,000 units a day intravenously for 9 days and 20,000 units intramuscularly every 2 hr for 3 days	Died with cardiac arrhythmia 2 mo after treatment	
8	16	F	7 mo	Teeth cleaned and filled	<i>Str viridans</i>	0.001	At another hospital the patient received a sulfonamide with typhoid chills and with malaria inocula; at this hospital she received 200,000 units of penicillin a day by constant intravenous drip for 20 days	Well	1 yr
9	17	F	2 mo	Tooth extractions	<i>Str viridans</i>	—	Penicillin 240,000 units a day by constant intravenous drip for 16 days	Well	1 yr
10	61	M	2 mo		<i>Str viridans</i>	0.080	Penicillin, 300,000 units a day by constant intravenous drip with sulfadiazine 1 gm every 4 hr for 13 days	Well, limited cardiac reserve	16 mo.
11	56	F	3 mo	Upper teeth pulled	<i>Str viridans</i>	0.080	Penicillin 300,000 units a day by constant intravenous drip with sulfadiazine 1 gm every 4 hr, for 22 days	Well further limitation in cardiac reserve	16 mo.
12	45	M	3 mo	Severe dental sepsis	<i>Str viridans</i>	0.035	Penicillin 300,000 units a day by constant intravenous drip for 22 days	Well	1 yr
13	27	F	2 mo	Tooth infection†	<i>Str viridans</i>	0.035-0.070	Penicillin 300,000 units a day by constant intravenous drip for 15 days; Penicillin 500,000 units a day by constant intravenous drip for 23 days; Penicillin 20,000 units intramuscularly every 2 hr with benzoic acid regimen for 30 days and 20,000 units intramuscularly every 3 hr with benzoic acid regimen for 30 days	Relapsed in 7 days; Relapsed in 2 wk.	9 mo

\*All patients had rheumatic heart disease except the one in Case 5 who had a postoperative infection following ligation of a patent ductus arteriosus; the one in Case 14 who had a bicuspid aortic valve and a patent ductus arteriosus and the one in Case 17 who had arteriosclerotic heart disease.

bolism, that complicated therapy in one of the above patients, as well as in another reported case.<sup>2</sup> The small size of this group and the rigid criteria for case selection probably account for the deviation in recovery from the usual 6 per cent rate reported elsewhere for sulfonamides alone.<sup>3</sup>

The most illuminating feature of our experience

temperature made in vivo therapy rational.<sup>6</sup> The most encouraging results were obtained in gonococcal and meningococcal infections.<sup>6</sup> Although a few patients with bacterial endocarditis due to *Streptococcus viridans* showed temporary improvement following short courses of fever therapy,<sup>7-9</sup> a cure was not brought about. The additional

finding that many strains of *Str viridans* recovered from the blood of patients with subacute bacterial endocarditis survived and grew in vitro at temperatures above those that the patient could tolerate<sup>7, 10</sup> furthered the neglect of fever treatment for this disease until Bierman and Baehr<sup>11</sup> reported their successes in 1941. In this hospital the use of fever

artificially induced fever by means of infrared radiation. It may be significant that this and other successful fever therapy cases underwent many more fever treatments than were used in the earlier failures with fever therapy alone. The first cure led to the unsuccessful treatment of 6 other patients in a similar fashion, and subsequently to the treatment

TABLE 1 (Continued)

CASE No	AGE	SEX	PROBABLE DURATION OF INFECTION	DENTAL HISTORY	SPECIES INFECTING ORGANISM	PENICILLIN SENSITIVITY	APPROXIMATE TREATMENT	RESULT	FOLLOW-UP
						units/cc			
14	20	M	5 mo		<i>Str viridans</i> <i>Alkalisigenes faecalis</i>	0.001 None	Penicillin 240 000 units a day intravenously for 9 days and 20 000 units intramuscularly every 2 hr for 13 days	Died	
15	32	M	4 mo	Infected tooth filled	<i>Str viridans</i>	0.035	Penicillin 500 000 units a day by constant intravenous drip for 14 days	Relapsed 4 mo later; died of ruptured spleen	
16	41	F	1 mo	Infected tooth†	<i>Str viridans</i>	0.035	Penicillin 300 000 units a day by constant intravenous drip for 20 days	Died 3 wk after treatment	
17	73	M	1 mo	No teeth	<i>Str faecalis</i>	0.035	Penicillin 20 000 units every 2 hr for 15 days and every 3 hr for 15 days with benzoic acid regimen	Died 3 wk after treatment of coronary occlusion	
18	62	M	10 days		Type 1 pneumococcus	—	Penicillin 300 000 units a day intravenously for 12 days; 20 000 units intramuscularly every 2 hr with 7.5 gm of benzoic acid thrice daily for 7 days and 20 000 units intramuscularly every 2 hr with 7.5 gm of benzoic acid thrice daily and low-salt and low-fluid intake for 30 days; Rest period for 15 days  Penicillin 20 000 units intramuscularly every 2 hr except 4.00 a.m. with benzoic acid and low-salt and low fluid intake, for 26 days	Relapsed; rise in temperature, hematuria, anemia rising sedimentation rate and negative blood culture  Well; acute congestive failure 10 wk later; good response to digitalis	7 mo
19	27	M	2 wk		<i>Str viridans</i>	0.007	Penicillin 500 000 units a day intravenously for 6 days (blood level 0.07 units per cc); 500 000 units a day intravenously for 7 days (blood level 0.14 units per cc) and 900 000 units a day intravenously for 9 days (blood level 0.20 units per cc)	Well	7 mo
20	19	F	4 wk		<i>Str viridans</i>	0.060	Penicillin 20 000 units intramuscularly every 2 hr for 9 days (blood levels 0.14, 0.14 and 0.07 units per cc); 40 000 units intramuscularly every 2 hr for 7 days (blood levels 0.14, 0.14 and 0.07 units per cc) and 80 000 units intramuscularly every 2 hr for 6 days (blood levels 0.28, 0.28 and 0.14 units per cc) all with benzoic acid 4 gm thrice daily and water limited to 1500 cc. and salt to less than 2 gm daily	Well	8 mo
21	47	M	3 wk	Abscessed tooth on physical examination	Alpha-hemolytic streptococcus	0.035	Penicillin 25 000 units every 2 hr intramuscularly for 28 days with benzoic acid 9.0 to 12.5 gm daily and low fluid and low-salt intake	Well; abscessed tooth removed during therapy	6 mo

†Painful obvious dental infection within 2 to 6 weeks before onset of present illness

therapy was begun because of the obvious improvement in one patient (Case 1) after drug fever of three days' duration had occurred during a course of sulfapyridine therapy (Table 1). Despite the fact that the responsible organism grew in the presence of 5 mg per cent sulfathiazole for twenty-four hours at 40°C, a cure followed a course of

of 9 more patients with typhoid vaccine as outlined by Solomon,<sup>12</sup> 3 of whom (Cases 2, 3 and 4) recovered. Through the stimulation of Osgood's<sup>13</sup> report, 2 of the patients listed above who received a sulfonamide without fever therapy were also given neoarsphenamine, and 1 patient (Case 6), treated with typhoid vaccine fever and a sulfonamide, was later

used In 2 of these cases continuous intravenous heparin was given in conjunction with oral sulfapyridine, and in 1 dicoumarin was given with sulfadiazine Heparin therapy was discontinued because of its apparent ineffectiveness, its cost and the difficulty of administration, and finally because of a fatal cerebral hemorrhage, probably due to em-

with the sulfonamides was their combination with fever therapy Although great interest in the use of artificially induced fever in the therapy of bacterial disease followed the meeting of the Fever Conference in 1935,<sup>4</sup> the emphasis in treatment remained on the diseases in which the in vitro sensitivity of the infecting organism to elevated

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CASE No	AGE	SEX	PROBABLE DURATION OF INFECTION	DENTAL HISTORY	SPECIES INFECTING ORGANISM	PENICILLIN SENSITIVITY	APPROXIMATE TREATMENT	RESULT	FOLLOW-UP
1	14	F	1 mo	Infected tooth†	<i>Str viridans</i>	—	Sulfapyridine, 1 gm every 4 hr for 11 days sulfathiazole, 1 gm every 4 hr, with 11 infra red treatments	Well	4 yr
2	25	M	19 days		<i>Str viridans</i>	—	Sulfadiazine, 1 gm every 4 hr, with 15 typhoid chills	Well	2 yr
3	25	M	2 mo	Gum infection	<i>Str viridans</i>	—	Sulfathiazole, 1 gm every 4 hr, sulfadiazine, 1.5 gm every 4 hr, with 10 typhoid chills	Well	3 yr
4	30	F	3 mo		<i>Str viridans</i>	—	Sulfadiazine, 1 gm every 4 hr, with 9 typhoid chills	Well	2 yr
5	20	F	1 mo		<i>Staph albus</i>	0.600-0.015	Penicillin 100,000 units a day by constant intravenous drip for 10 days and 8300 units intramuscularly every 3 hr for 9 days Sulfadiazine 1 gm thrice daily, maintenance dose Penicillin 300,000 units a day by constant intravenous drip for 11 days and 50,000 units every 2 hr intramuscularly for 10 days	Relapsed in 6 wk.  Relapsed in 2 mo and died from an other cause 10 mo later	
6	52	F	3 mo  10 mo		<i>Str viridans</i>	—	Sulfadiazine, 1 gm every 4 hr, with 5 typhoid chills, sulfadiazine 1 gm every 4 hr and neocarsphenamine 400 mg, with 7 typhoid chills Penicillin 240,000 units a day by constant intravenous drip for 12 days	Well subsequent heart failure	1 yr
7	38	M	10 wk		<i>Str viridans</i>	—	Penicillin 240,000 units a day intravenously for 9 days and 20,000 units intramuscularly every 2 hr for 3 days	Died with cardiac arrhythmia 2 mo. after treatment	
8	16	F	7 mo	Teeth cleaned and filled	<i>Str viridans</i>	0.001	At another hospital the patient received a sulfonamide with typhoid chills and with malaria inocula at this hospital she received 200,000 units of penicillin a day by constant intravenous drip for 20 days	Well	1 yr
9	17	F	2 mo	Tooth extractions	<i>Str viridans</i>	—	Penicillin 240,000 units a day by constant intravenous drip for 16 days	Well	1 yr
10	61	M	2 mo		<i>Str viridans</i>	0.080	Penicillin, 300,000 units a day by constant intravenous drip with sulfadiazine 1 gm every 4 hr for 13 days	Well limited cardiac reserve	16 mo.
11	56	F	3 mo	Upper teeth pulled	<i>Str viridans</i>	0.080	Penicillin 300,000 units a day by constant intravenous drip with sulfadiazine 1 gm every 4 hr, for 22 days	Well further limitation in cardiac reserve	16 mo.
12	45	M	3 mo	Severe dental sepsis	<i>Str viridans</i>	0.035	Penicillin 300,000 units a day by constant intravenous drip for 22 days	Well	1 yr
13	27	F	2 mo	Tooth infection†	<i>Str viridans</i>	0.035-0.070	Penicillin 300,000 units a day by constant intravenous drip, for 15 days Penicillin 300,000 units a day by constant intravenous drip for 23 days Penicillin 20,000 units intramuscularly every 2 hr with benzoic acid regimen for 30 days and 20,000 units intramuscularly every 3 hr with benzoic acid regimen for 30 days	Relapsed in 7 days Relapsed in 2 wk.  Well	9 mo.

\*All patients had rheumatic heart disease except the one in Case 5 who had a postoperative infection following ligation of a patent ductus arteriosus, the one in Case 14 who had a bicuspid aortic valve and a patent ductus arteriosus and the one in Case 17, who had arteriosclerotic heart disease

bolism, that complicated therapy in one of the above patients, as well as in another reported case.<sup>2</sup> The small size of this group and the rigid criteria for case selection probably account for the deviation in recovery from the usual 6 per cent rate reported elsewhere for sulfonamides alone.<sup>3</sup>

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temperature made in vivo therapy rational.<sup>5</sup> The most encouraging results were obtained in gonococcal and meningococcal infections.<sup>6</sup> Although a few patients with bacterial endocarditis due to *Streptococcus viridans* showed temporary improvement following short courses of fever therapy,<sup>7-9</sup> a cure was not brought about. The additional

20,000 units every three hours for fifteen days more. With this schedule the salt intake was restricted to less than 3 gm a day, fluids were restricted to less than 1500 cc a day, and 2.5 gm of benzoic acid in capsules was given three times a day with meals. During therapy the patient remained on the benzoic acid regimen.<sup>18</sup> At autopsy a healing vegetation measuring 1 cm by 3 cm by 0.1 cm was found firmly attached to the closure line of an aortic cusp. It contained no bacteria on smear, culture or microscopic examination of sections. The cause of death was acute coronary occlusion, possibly due to temporary obstruction of the left coronary orifice by the curtainlike vegetation.

The sixth death (Case 5) occurred in May, 1945, following a massive hemorrhage from a bronchus. The endocarditis had developed as a postoperative complication of an unsuccessful ligation of a patent ductus arteriosus. This hemorrhage occurred seven months after the first course of penicillin and nine months after all evidence of infection had disappeared. Autopsy revealed the original patent ductus arteriosus opening into a large aneurysmal sac in the pulmonary artery and a silver clip eroding a small branch of the pulmonary artery and the adjacent bronchus. Apparently one of the clips used in the ligation had been engulfed by the subsequent aneurysm and had been carried by the blood stream to the lung. There was complete healing of the mediastinum and vascular walls.

Two of these deaths (Cases 5 and 17), were in cases of proved bacteriologic cure, and in 1 (Case 7) the patient may have been free of vegetations.

#### DENTAL ASPECTS

Although isolated cases of subacute bacterial endocarditis following tooth extractions have been known for some years, it is only recently that the great significance of this factor has been appreciated. That bacteremia follows tooth extractions in 70 per cent of cases,<sup>19</sup> frequently follows minor dental manipulations and may occur after the simple act of chewing has been established.<sup>20</sup> In this series of 347 cases the perfunctory dental histories of the routine records have revealed an incidence of tooth extractions in 10 per cent of the cases and other dental manipulations in an additional 10 per cent within several weeks before the onset of bacterial endocarditis. During the past two years, in which there has been a deliberate inquiry about dental sepsis as a part of the patient's present illness, its real importance has been demonstrated (Table 1). Among earlier patients numerous other foci of infection and a variety of surgical procedures have similarly acted as the origin of this infection — namely, tonsillectomy, sequestrectomy, abdominal operations (appendectomy, colostomy, tubo-oophorectomy and so forth), prostatic massage and others. Nevertheless, dental sepsis is the most prominent

offender. The significance of this factor is emphasized by bacteriologic differentiation of the causative organisms. Most edentulous patients who develop bacterial endocarditis are infected with the enterococcus, the staphylococcus or even the gonococcus, whereas the overwhelming majority of patients who still have their teeth are infected with *Str. viridans*, which is so generally associated with dental sepsis and the bacteremia attending dental procedures. It is because of these findings in patients with subacute bacterial endocarditis who need dentistry that we have completed necessary dental extractions and manipulations while the patients have been receiving penicillin, and have continued therapy until gum healing is complete. When the teeth are so poor as to constitute a subsequent threat of reinfection of the heart valves, we have removed all of them before completing treatment.

#### STREPTOCOCCUS SKIN TESTS

A final point of interest is the skin reaction to intradermal injections of streptococcus nucleoprotein. It is known that 85 per cent of cases of rheumatic fever show a positive reaction to beta-hemolytic streptococcus skin tests.<sup>21</sup> It is the finding of others<sup>22-23</sup> and it has been our experience<sup>24</sup> that cases of subacute bacterial endocarditis rarely show such positive skin reactions. Post-mortem evidence of concurrent active rheumatic carditis and subacute bacterial endocarditis is not necessarily a contradictory finding, for there is reason to believe that the rheumatic state can be activated by or follow and need not precede the bacterial endocarditis.<sup>25</sup>

At present the streptococcus skin test is a useful empirical diagnostic tool. Seventy-four of 77 patients with undoubted bacterial endocarditis have had negative beta-hemolytic streptococcus skin tests, and all 77 have had negative alpha-hemolytic streptococcus skin tests.\* Eleven patients who had negative skin tests during active bacteremia developed positive alpha-hemolytic and beta-hemolytic streptococcus skin tests, either during or shortly after penicillin therapy, and have so far maintained their positive reactions.

#### DISCUSSION

It is fair to point out that all but 1 of the deaths following penicillin therapy were due to causes beyond the control of this drug. The successes, although not so fraught with bizarre complications as were the fatal cases, nevertheless were gained despite chronicity of the disease and advanced age, great debility and poor cardiac reserve of the patients. One patient (Case 6) developed congestive heart failure and had a cerebral hemorrhage or embolus during an unsuccessful course of fever and sulfonamide therapy several months before penicillin

\*Details of these data will be presented elsewhere in a subsequent publication.

given typhoid vaccine, sulfadiazine and neoarsphenamine simultaneously. No one of these last 3 patients was cured by such desperate measures, whereas 1 (Case 6) was subsequently readily cured with a short course of penicillin.

When fever was induced by infra-red radiation, the rectal temperature was kept at 105 to 106°F (40.6 to 41.1°C) for three to five hours for eight or more treatments on alternate days. For typhoid-vaccine fever, 25,000,000 typhoid-paratyphoid organisms were injected intravenously for the first dose, and the amount was doubled at intervals of two or three days. The purpose was to obtain a temperature of 104°F (40.0°C) for several hours. Ten or twelve such treatments were usually given. In some cases the amount of vaccine was increased or decreased because the response was insufficient or excessive. Of the 16 patients who had this combination of fever and sulfonamide therapy, there were cures in 4 (Cases 1, 2, 3 and 4)\* — the first such cures ever obtained in this hospital. These recoveries with combined fever and sulfonamide therapy are in accord with the ratio 4/25 reported elsewhere for hyperthermia<sup>8</sup> and that of 5/17 for typhoid-vaccine fever and sulfonamides.<sup>12</sup>

#### PENICILLIN ERA

Of the 20 cases treated in the third period, 17 (Table 1) received adequate courses of penicillin, 2 were diagnosed post mortem, and in 1 no treatment was given because the patient was in terminal uremia on admission and the limited drug supply at the time did not justify treatment of an apparently hopeless case. Penicillin was given for two to four weeks in a constant intravenous drip of 5 per cent dextrose at the rate of 240,000 to 500,000 units a day. At the time of this writing, six to eighteen months following treatment, 11 of the 17 adequately treated cases are cured or arrested and 1 patient (Case 5) has been cured but has died of another cause. Three of these 11 patients (Cases 5, 13 and 18) required more than one course of penicillin. In 2 of the 17 adequately treated cases (Cases 10 and 11), sulfadiazine was given with penicillin. In a word, in 11 of the 17 well authenticated cases of subacute bacterial endocarditis the patients have responded favorably to penicillin therapy and have remained well for six to eighteen months.

Each of the 6 patients who died after adequate penicillin therapy presented a complicated problem. One (Case 7) died of congestive heart failure two months after penicillin was stopped. In the interval between treatment and death, auricular fibrillation, sweating and a rapid heart rate were present. During this time the patient remained afebrile and the blood cultures were sterile. Unfortunately, the

cause of death is not known, for the patient died at home and no post-mortem examination was made.

The second patient (Case 14) died of general septicemia three weeks after penicillin treatment was stopped. Repeated blood cultures before treatment contained *Str. viridans*. When penicillin was begun this organism disappeared from the blood, and it was not recovered again during life or from the post-mortem heart's blood. After a week of penicillin, a gram-negative bacillus, *Alkaligenes faecalis*, appeared in the blood cultures and persisted until death, despite further penicillin and later sulfadiazine therapy. At autopsy, both *Str. viridans* and *Al. faecalis* were cultured from vegetations found on a bicuspid aortic valve and a patent ductus arteriosus.

The third patient (Case 16), with a short illness had a positive streptococcus skin test on admission that became negative before treatment and during active bacteremia. The only clinical response to penicillin given by constant intravenous drip was control of embolic phenomena and bacteremia. High fever and debility persisted. After penicillin was discontinued, the blood cultures remained negative until death three weeks later. In this interval dermatitis exfoliativa and acute yellow atrophy appeared. At autopsy healing vegetations were found that when crushed and cultured yielded the same type of streptococcus as that found in life. In retrospect this patient was probably inadequately treated. We have since found it necessary to raise the penicillin dose by steps to well over 1,000,000 units a day to control systemic symptoms of the septicemia. When even this dose is inadequate, the addition of the benzoic acid regimen gives blood levels equivalent to a daily dose of 6,000,000 to 10,000,000 units a day.

The fourth patient (Case 15) responded favorably to a two-week course of 300,000 units of penicillin a day by constant intravenous drip. He remained well until four months later, when a splenic infarct took place and a low-grade fever appeared. Death from a ruptured spleen occurred two weeks later during an interval in which repeated negative blood cultures delayed the reinstitution of penicillin therapy. At autopsy, healed and healing vegetations were found that contained *Str. faecalis* by smear and culture. The splenic infarct was sterile. The infecting organism was different from the one recovered during the first illness, and this fact invites speculation whether the patient died of a reinfection rather than of a recurrence. A ruptured spleen in subacute bacterial endocarditis is infrequent.<sup>14-16</sup> This case will be reported in detail elsewhere.<sup>17</sup>

In the fifth case (Case 17), death occurred suddenly three weeks following thirty days of penicillin therapy — 20,000 units every two hours day and night intramuscularly for the first fifteen days and

\*Another patient recovered with sulfadiazine and typhoid vaccine therapy but was not included because blood cultures were always negative although he showed many of the other clinical features of bacterial endocarditis.

in other patients when the pattern of their illness was favorable as judged by symptoms, temperature, a rise in hemoglobin, a fall in the sedimentation rate and clearing of the urine. The change of the streptococcus skin reaction to positive usually occurred before treatment was discontinued and was interpreted as a favorable sign. One patient (Case 13), however, relapsed after such a change, and 1 (Case 19) did not have a positive reaction until some weeks after treatment but nevertheless recovered. In this series recovery has followed two weeks of treatment in some cases, as in Case 6, and as long as two months of treatment in others, as in Case 13.

With special attention to the penicillin dosage in subacute bacterial endocarditis, it should be possible to raise the recovery ratio to an even higher figure than that of 11/17 in this study, especially when the disease is recognized early, the organism is found to be sensitive to a certain level of penicillin and the dosage is planned accordingly.

#### SUMMARY

Three hundred and forty-seven proved cases of subacute bacterial endocarditis treated at the Peter Bent Brigham Hospital from 1913 to 1945 have been studied. There were no known recoveries among 237 cases seen between 1913 and 1937, during which time a great variety of therapeutic procedures were employed.

Of the 90 cases observed from 1937 to 1943, 55 received adequate treatment with a sulfonamide. Sixteen of the latter patients were given simultaneous fever therapy. Of these, 1 treated by infrared radiation and 3 treated by typhoid vaccine recovered and have remained well for two to four years. None of the other sulfonamide-treated patients recovered.

Of 20 patients studied since January, 1944, 17 were given large doses of penicillin. In 11 cases the infection has been cured or arrested, and the patients are now alive. The follow-up periods vary between six and eighteen months. In two others the infection was bacteriologically arrested but death occurred some weeks later because of complications.

Congestive heart failure may follow recovery from the infection.

Dental sepsis, extraction of teeth and dental manipulations were found to be related to the onset of this disease in a surprisingly large number of cases. Infected teeth should be removed before treatment is completed, as a prophylaxis against subsequent reinfection of the heart valves.

A change in the sensitivity of the skin to streptococci was found to vary with the stage of illness. The reaction was almost invariably negative during the active stage of infection (74 of 77 cases) and became positive in the patients who recovered (11 cases).

Although penicillin appears to be a promising cure for subacute bacterial endocarditis, patients who recover from this disease are left with the same or further valvular deformities, which continue to predispose them to reinfection or to subsequent congestive heart failure.

The successful treatment of a patient with subacute bacterial endocarditis is an individual problem that requires careful attention to the details of therapy. Successful treatment depends on maintaining penicillin blood levels considerably in excess of the minimal inhibiting concentration of penicillin for the patient's organism.

Abstracts of the 4 cases successfully treated with sulfonamides and of 14 of the 20 cases treated with penicillin will appear in the reprints of this paper.

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was administered. Although now ambulatory, she is on constant digitalis therapy and suffers primarily from moderate congestive failure. Another patient (Case 10) was in congestive failure when the diagnosis of bacterial endocarditis was first made. Since recovery he has had two bouts of mild congestive failure without evidence of infection. A third patient (Case 8) was of interest because she showed evidence of acute nephritis before treatment. The urine contained considerable albumin and many red cells, white cells and casts. There was marked anemia, with a red-cell count of 2,600,000. Despite the severity of the illness, the response to treatment was most satisfactory. A fourth patient (Case 15) did well up to his recurrence or reinfection four months later, although before treatment he had had a cerebral embolism with hemiplegia. Functional recovery of the affected side of the body was almost complete. One patient (Case 2) treated with sulfadiazine and fever and 6 patients (Cases 5, 9, 10, 14, 18 and 20) treated with penicillin had arterial emboli after therapy had been stopped, but despite these did well. The inference to be drawn is that sterile emboli may occur without preventing a favorable outcome. It is also important that the physician be not unduly disturbed at unexpected rises in temperature during the course of treatment, because these are often due to local phlebitis at the site of the constant intravenous injection. He should, however, be concerned by a continuous fever during therapy, because this usually means inadequate amounts or methods of giving penicillin — as in Case 16. Another point of considerable significance is the fact of recovery in several cases even though treatment was begun many months after the onset of the disease and in spite of the patients' advanced age. It is obvious that the outlook is better when the diagnosis is made promptly, but it is comforting to know that favorable results can be obtained in patients who have been neglected for six months or more, as in Cases 6 and 8.

Studies with the streptococcus skin tests were of special interest in the penicillin-treated patients. At the present time one may speculate that whatever the state of immunity or sensitivity of the host to streptococcal infections before the development of bacterial endocarditis, the bacteremia effectively desensitizes as well as immunizes the host during infection. The prompt control of septicemia and splenomegaly and the early appearance of a positive streptococcus skin reaction during or following penicillin therapy suggest that the principal effect of this drug is to localize the valvular infection. The finding of viable streptococci in the valves in fatal cases that had received relatively short courses of penicillin (Cases 14, 15 and 16) and not in a patient treated for one month (Case 17) suggests that at least two, often three or four and sometimes even eight weeks of penicillin — as in Case 13 —

are necessary before the vegetations heal completely. Recurrent sterile emboli appearing during and shortly after treatment give further support to this theory. In the fatal case with a curtainlike vegetation (Case 17) the patient might well have had a sterile embolus during convalescence had he not died of another condition.

The use of large doses of penicillin in the treatment of subacute bacterial endocarditis was introduced by Loewe.<sup>26</sup> The aim of therapy is the maintenance of a penicillin blood level considerably in excess of the minimal inhibiting concentration for the patient's organism for an extended period of time. A higher level maintained for a short time does not seem to be an effective alternative mode of treatment, Case 13 is an example. Two hundred thousand or 300,000 units a day given either by constant intravenous drip or by two-hourly intramuscular injections day and night may serve to maintain such a level in the blood stream most of the time,<sup>27</sup> and do so continuously when combined with the benzoic acid regimen.<sup>18</sup> Patients with a free aortic regurgitation may require as much as 1,000,000 units a day to maintain equivalent blood levels. The patient in Case 19 was treated by the constant intravenous drip method and the one in Case 20 with the benzoic acid regimen and intramuscular injections every two hours. In the latter patient it was found to be practical to give up to 80,000 units in 2 cc of saline solution, and this was done without any more local discomfort than is experienced with the usual dose of 20,000 units in 4 cc of saline solution. Despite these doses, the blood levels did not exceed fivefold the minimal penicillin concentration that inhibited their respective organisms.

Because of the importance of individualizing the treatment of subacute bacterial endocarditis, whenever possible we have determined the penicillin sensitivity of the patient's organisms and gauged the necessary amount of therapy by the lowest penicillin blood levels attained in treatment. From the cases covered in this report it appears that a blood level that remains just above or often falls below the minimal inhibiting concentration for the bacteria does not control symptoms or temperature. A good working rule is to maintain a blood level five or more times the minimal effective level. Just how this is to be done varies with the patient. By the same token, no set rules for the duration of therapy can be stated. In Case 13 the patient relapsed twice, both times after apparently adequate therapy. When therapy was continued the third time until the sedimentation rate had fallen close to normal, she recovered. The patient in Case 18 relapsed but responded to retreatment which was continued until after the microscopic hematuria was controlled. The sedimentation rate was not normal but became stabilized at a somewhat elevated level. Penicillin was discontinued

Each of these valuable adjuncts, however, has been enthusiastically ushered in, only to be later ranked as falling far short of being the unmixed blessing it seemed at first. Certainly, few can deny that the efficient care of obstructed patients calls for nicety of judgment, assiduous and diligent attention and individualization hardly demanded by any other group. Such cases do not lend themselves to standardization by any known therapeutic scale. It is with this precept in mind, rather than varying formulas of duration of obstruction, objective findings of abdominal tenderness, rigidity and the like or white-cell counts, that one should attempt to treat these patients.

Any series of acute intestinal cases with an unusually low mortality of necessity demands an accounting of the methods of diagnosis employed. Little question of diagnostic accuracy is encountered in the patients receiving operations, the finding in whom of obliteration of a section of bowel lumen, with dilatation of the bowel above and its collapse below the point, eliminates argument concerning classification. Justifiable critical scrutiny, however, may be aimed at the cases not operated on. Only one of our patients with hernial obstructions was not operated on, the ultimate diagnosis being confirmed at autopsy. This method of confirmation was applied to a case of obstruction due to a metastatic malignancy and to another due to mesenteric vascular occlusion. With the exception of these

admission and after two or more irritating enemas, typical peristalsis and roentgenologic demonstration of distended bowel, with fluid levels and absence of colonic gas. Failure to demonstrate any one or more of these diagnostic points has excluded many cases from the series.

Paramount in the criteria for judging the method of handling these problems is an assessment of the general condition rather than the local disease. We fear, as do all surgeons, the progression of bowel changes from obstruction to strangulation and finally to loss of viability, but we also believe these to be relatively overemphasized. We are convinced that it is better to operate on many of these patients six, eight or ten hours later, when they can tolerate the procedure, than to perform a possibly simpler and easier operation at once when they are too ill to stand it. We believe that it is safer to consider every patient with intestinal obstruction as critically ill and as a truly poor-risk patient, one who is actually too ill to withstand the operation that he nonetheless may require. Therefore, we do not allow our natural fear of local bowel change to carry the same weight as concern for the patient's general condition. The former is more obvious, more easily demonstrated and more readily evaluated, but the latter constitutes the greater threat to life.

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Inguinal	23	12	2	1	2	4	8
Femoral	5	5	1	1	1	20	20
Postoperative	3	1	0	0	0	0	0
Internal	5	5	1	0	0	0	0
Postoperative adhesions	22	2	1	1	1	5	2
Inflammatory adhesions	6	1	0	1	1	17	11
Intussusception	5	5	0	0	0	0	0
Volvulus	5	5	1	0	0	0	0
Mesenteric vascular occlusion	2	2	0	2	3	100	100
Carcinoma							
Metastasis	1	0	1	0	1	0	0
Primary malignancy	1	0	1	0	0	0	0
Meckel's diverticulum	1	0	1	0	0	0	0
Regional ileitis	2	0	2	0	0	0	0
Tuberculosis of ileum	1	0	1	0	0	0	0
Totals	90	43	14	7	10		
Percentages						7.7	8.4

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condition when the patient has reached the peak of general systemic improvement. Of course, some of these patients seek hospital care quite early in their illness, often permitting immediate surgery, but their number in municipal institutions is notably small. Even this group, however, receives what might be called prophylactic treatment for shock, intubation, suction and blood or plasma before and during operation, despite their apparently satisfactory condition on admission. The other, much larger, group demands an exhaustive study to assess its ability to counter the shocking effect of the

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## A Report of One Hundred and Eighteen Cases

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WASHINGTON, D C

HOSPITALS devoted to the care of charity patients are not usually expected to be sources of low mortality rates. The reasons for this, which are many and varied, include the generally poor state of nutrition among these patients, their ad-

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It appears from an analysis of such results as are reported that a rate of about 20 per cent is a reasonable goal at which to aim. To illustrate this consensus, the mortality rates from some leading clinics are presented in Table 1.

Richardson<sup>12</sup> indicts acute obstruction for causing half as many deaths as its far more frequent competitor, acute appendicitis with sequelae, and assigns to it a mortality of 40 to 60 per cent in the United States in 1944. Colcock<sup>13</sup> terms it "the most serious lesion affecting the small bowel." Stone and Owings<sup>14</sup> write that the results of its treatment are unsatisfactory and that the mortality is unnecessarily high. Dennis and Brown<sup>10</sup> in 1943 summarized the general mortality up to the time of their report as 18 to 20 per cent in skilled hands. Thus, the gravity of this problem is emphasized directly or indirectly by all authors, and it is undeniable that the problem of management of these patients is far from solved. The tragedy of such

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Hernia				yr	x10 <sup>3</sup>			%
Umbilical	8	4 hr-6 days	50 hr	48	17 0	96	100 2	50
Inguinal	24	3 hr-9 days	14 hr	44	16 0	98	99 8	67
Femoral	5	14 hr-6 days	28 hr	69	11 0	70	98 0	—
Postoperative ventral	3	6 hr-4 days	22 hr	41	9 0	116	99 4	67
Internal	5	7 hr-4 days	40 hr	39	13 0	100	100 8	100
Postoperative adhesions	44	3 hr-9 days	38 hr	37	12 0	106	101 4	93
Inflammatory adhesions	9	10 hr-14 days	32 hr	32	18 0	110	101 4	89
Intussusception	5	3 hr-38 hr	16 hr	1	9 0	?	100 8	50
Volvulus	5	1 1/2 hr-30 hr	18 hr	49	21 0	118	101 2	—
Mesenteric vascular occlusion	3	22 hr-5 days	58 hr	67	23 0	104	97 8	100
Carcinoma:								
Metastasis	2	15-24 days	8 days	53	7 0	76	98 6	100
Primary malignancy	1	34 hr	34 hr	50	6 0	82	98 0	100
Meckel's diverticulum	1	16 days	16 days	53	13 0	102	99 6	100
Regional ileitis	2	18 hr-36 hr	27 hr	36	8 0	90	98 2	100
Tuberculosis of ileum	1	3 days	3 days	41	7 0	88	98 0	100
Total	118							
Averages			64 hr	46	15 6	102	100 3	85

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Before what might be called the "Wangensteen era," the last decade or so—the prognosis of acute intestinal obstruction was truly grave. Miller<sup>1</sup> reported a mortality of 61 per cent in 1929. Cole<sup>2</sup> states that the mortality of two decades ago was 30 to 40 per cent. Bennett<sup>3</sup> states that a 70 per cent mortality prevailed in earlier days. Moreover, a survey of the more recent literature reveals that

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During the last fifteen years great forward strides have been made in the management of these problems. These have been accomplished through such procedures as the Wangenstein<sup>6, 15</sup> suction method, the Miller-Abbott<sup>16</sup> intubation method, Fine's<sup>17</sup> oxygen decompression method and the liberal use of parenteral fluids, blood and plasma,<sup>2, 8, 9, 11, 18-20</sup> to mention the more dramatic advances

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Femoral	5	5	1	1	1	20	20
Postoperative	3	1	0	0	0	0	0
Internal	5	5	1	0	0	0	0
Postoperative adhesions	22	2	1	1	1	5	2
Inflammatory adhesions	6	1	0	1	1	17	11
Intussusception	5	5	0	0	0	0	0
Volvulus	5	5	1	0	0	0	0
Mesenteric vascular occlusion	2	2	0	2	3	100	100
Carcinoma							
Metastasis	1	0	1	0	1	0	0
Primary malignancy	1	0	1	0	0	0	0
Meckel's diverticulum	1	0	1	0	0	0	0
Regional ileitis	2	0	2	0	0	0	0
Tuberculosis of ileum	1	0	1	0	0	0	0
Totals	90	43	14	7	10		
Percentages						7.7	8.4

cases and of those due to adhesions, all our diagnoses were confirmed at operation. Concerning the cases due to adhesions, the presence of complete obstruction may be difficult to decide with certainty without operation, and many patients who were treated conservatively have been omitted from this survey because there was a lack of one or more absolute criteria for the conclusion that obstruction was complete. Of this group of patients, 22 satisfied our criteria by the demonstration of intermittent, cramping abdominal pain, repeated vomiting, failure to pass gas or feces by rectum prior to

condition when the patient has reached the peak of general systemic improvement. Of course, some of these patients seek hospital care quite early in their illness, often permitting immediate surgery, but their number in municipal institutions is notably small. Even this group, however, receives what might be called prophylactic treatment for shock, intubation, suction and blood or plasma before and during operation, despite their apparently satisfactory condition on admission. The other, much larger, group demands an exhaustive study to assess its ability to counter the shocking effect of the

contemplated operation. It is difficult to make blanket recommendations for judging this ability, but generally speaking we favor postponing surgery until the pulse is stabilized below 110, the blood pressure is at normal or near-normal limits, the acid-base balance is restored, as estimated by the type of respiration, the plasma carbon dioxide combining power, acetonuria, dermination of the serum sodium and chloride levels and so forth, hydration has been achieved, as determined by the appearance and feel of the tongue, blood urea nitrogen studies, the specific gravity and quantity of urine passed during preparation and hematocrit studies, the definitive treatment of complications, such as pneumonia and heart failure, is well under way, there is significant improvement in distention, and the general effects of shock — sweating, pallor or cyanosis, coldness of the extremities and mental torpor or severe anxiety — have been alleviated.

To illustrate the importance and frequent association of these factors in the present series, certain facts are of interest. Of the 90 patients undergoing operation, only 9 (10 per cent) were admitted with pulse rates below 90. Eleven (12 per cent) were admitted with a pulse in excess of 120 and a systolic blood pressure below 100. Three (3 per cent) were admitted with no radial pulse or blood pressure detectable. Of these, 1 patient, a fifty-eight-year-old man with a strangulated inguinal hernia of eight days' duration, died. He was operated on after six hours of preparation with a systolic blood pressure of only 80 because no more blood or plasma was available. This was the only patient in this group of 11 admitted in shock who had not been restored from it before operation.

At this point there arises the question so often propounded concerning the hypothetical patient who does not respond favorably to the giving of blood or plasma, suction and so forth during the preparative period. These conditions exist very rarely when enough preparation is given. Even in the 3 patients with complete occlusion of the superior mesenteric artery, only 1 failed to respond favorably and was therefore not operated on. A girl of seventeen, who had had obstruction from postinflammatory adhesions for fourteen days, required 4800 cc of blood and plasma in eighteen hours to stabilize the pulse and blood pressure and who was mistakenly declared dead by an intern shortly after admission, had an uneventful postoperative course. Even the rare patient who does not respond leaves one no alternative, however, since an anesthetic and a major operation would certainly not alleviate the state of shock.

Only 9 patients (10 per cent) were admitted within twenty-four hours of the onset of obstruction, as contrasted with 44 per cent reported by Dennis and Brown,<sup>10</sup> with a 78 per cent mortality. There was no mortality in our comparable group.

Disturbances in acid-base balance were almost the rule, being evidenced by acetonuria, depletion of serum chloride and so forth in 86 per cent of the cases tested. Major degrees of dehydration, manifested by a dry tongue, scanty and concentrated urine, excessive blood concentration and elevated blood urea nitrogen, were observed in 43 per cent of the series. Four patients (4 per cent) had pneumonia complicating the obstruction, 5 (6 per cent) had coincident cardiac failure, and 3 others had a systolic blood pressure in excess of 200.

From these data it will be seen that the recent recommendations for early or immediate operation<sup>3, 8, 12, 14, 16, 21, 22</sup> could not be applied to the type of patient seen in this hospital. The operation for intestinal obstruction, however simple, is made on a patient poorly constituted to tolerate it, who requires a considerable amount of care to provide reasonable assurance of his survival.

During the period from January 1, 1943, to March 1, 1945, a total of 118 cases of small-bowel obstruction were observed (Table 2). Ten of these patients died, a mortality of 8 per cent. Ninety patients were operated on, and 7 of these died, a mortality of 8 per cent. In 14 patients resection was necessary, and 3 of these died, a mortality of 21 per cent. The operations in all cases with resection, with one exception, consisted of a primary anastomosis of the aseptic type. In 2 of the fatal cases, massive gangrene of the small bowel, caused by mesenteric vascular occlusion, was found, but resection was not performed.

#### SUMMARY AND CONCLUSIONS

One hundred and eighteen cases of acute complete small-bowel obstruction seen in a large municipal hospital, 90 of whom were treated operatively, are presented. Data of interest on these patients are given.

The generally high mortality in this group, from several decades past to recent reports from leading clinics, is reviewed.

The necessity for evaluation of the patient as a whole rather than placing undue emphasis on local bowel disease is stressed.

A warning note is sounded against the preponderant recent advocations of immediate operation on these severely ill patients, and a plan for evaluating the proper time for operation is presented.

The general nature of the systemic condition of these patients is summarized.

Of the 118 patients treated, 10 died, a mortality of 8 per cent. Of the 90 operated on, 7 failed to survive, an operative mortality of 8 per cent.

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## EPISTAXIS\*

HENRY H AMSDEN, M D

CONCORD, NEW HAMPSHIRE

**N**OSEBLEED is of frequent occurrence, often stops spontaneously and in the great majority of cases is easily controlled. It may, however, be extremely persistent and, although seldom endangering life, may cause much anxiety to both patient and physician.

In the event of persistent or recurring attacks, a search should be made for some underlying cause, such as hemophilia, leukemia, anemia or diabetes. This type of nosebleed also frequently occurs in hypertension in elderly people and in affections caused by hemolytic streptococci. It should be regarded as a surgical condition, and the usual measures should be taken for its control, through direct pressure, cauterization or cutting off the blood supply to the bleeding point, by ligation or otherwise.

A study of the anatomy of the blood supply of the nose affords a more intelligent approach to treatment. The sphenopalatine artery is a branch of the internal maxillary, which in turn is derived from the external carotid. This artery comes through the sphenopalatine foramen, and its terminal branches are distributed over the septal and lateral walls of the nasal cavity. A large branch runs along the floor of the nose and anastomoses with the great palatine artery through the incisive foramen.

A large majority of spontaneous hemorrhages occur from the so-called "Kisselbach's area," an arteriovenous plexus on the anteroinferior portion of the cartilaginous septum. These vary from simple oozing, easily controlled by pressure, to active arterial bleeding from a small vessel.

Various means of control have been advocated, among them pressure with packs saturated with hydrogen peroxide or adrenalin, the application of salt pork, fresh tonsillar tissue, snake venom and various hemostatic preparations and the submucous injection of novocain. The use of an inflated glove finger has also been suggested.

The simplest and most efficient method, when the bleeding point can be readily seen, is direct cauterization of the anesthetized mucous membrane. Care should be taken not to burn too deeply, thus perforating the opposite nostril. In some cases of mild bleeding a crystal of chromic acid fused on a metal applicator is sufficient.

The most annoying type of bleeding comes from some point that cannot readily be seen, and for which other means of control must be adopted. Bleeding may occur from a point on the posterior surface of a septal deviation not accessible to cauterization, this can be controlled by submucous resection. In recurring bleeding from Kisselbach's area, it may be unwise to repeat cauterization, and submucous elevation of the mucoperichondrium may be necessary.

Most spontaneous hemorrhages — that is, those of the nontraumatic variety — seem to come from a point below the level of the inferior turbinate, they seldom arise from the upper portion of the nasal cavity. The postnasal plug, sometimes necessary, is extremely annoying to the patient and may lead to infection of the middle ear or sinuses, the plug should ordinarily not be left in place for more than twenty-four hours. The best method of inserting it is as follows. A soft catheter introduced through the bleeding nostril is drawn out through the mouth, and a double string is attached to the

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catheter and withdrawn through the nose, pulling the plug into place. The nostril should be tightly packed and the double string tied over a sponge, a third short string attached to the plug facilitates its removal through the mouth.

Before resorting to this method, an effort should be made to locate more accurately the source of the bleeding. As already stated, most of these hemorrhages seem to come from a point below the lower turbinate. It is difficult to pack gauze into this area, and a useful procedure is to introduce several wooden applicators wound with cotton and saturated with adrenalin or cocaine, this in itself often stops the bleeding and helps to locate its source. The applicators may be left in place for some time if desired.

Reference to the blood supply of the nose shows that the largest arterial vessel is the anastomosis between the sphenopalatine and great palatine arteries through the incisive foramen, and it is at this point

that persistent hemorrhage may occur. In fact, active pulsation is often seen here, at a point inaccessible to cauterization. A method that has proved successful in meeting this situation is submucous elevation of the tissue on the floor of the nose and lower meatus. Under novocain anesthesia an incision is made at the mucocutaneous juncture, allowing the insertion of a sharp submucous elevator carrying the separation back beyond the incisive foramen, thus shutting off the blood supply. If necessary, a small gauze pack may be inserted between the soft tissues and the bone. In case the hemorrhage cannot be controlled in the manner suggested, it may be necessary to tie off the external carotid artery.

#### SUMMARY

Methods for the control of persistent or recurring epistaxis are reviewed.

## CARDIOVASCULAR DISEASE AMONG VETERANS OF WORLD WAR II\*

### A Survey of 19,870 Cases

MAJOR AARON H. TRAUM, M.C., A.U.S.,† AND BLANCHE B. WILCOX, Ph.D.‡

With the technical assistance of the Office of Budget and Statistics

WASHINGTON, D. C.

**T**HERE are many gaps in the knowledge of heart disease, the leading cause of death among adults in the United States. To follow a case of cardiovascular disease from its earliest recognized manifestations throughout the lifetime of the patient may lead to a better understanding of such disease processes. Furthermore, there is a distinct need for more information concerning the natural history of circulatory disturbances that apparently commence or exhibit their first signs and symptoms in young adults. The relation of race, sex, age, place of residence and similar factors to various types of heart disease can best be appraised by analyzing and following large numbers of cases in each disease category.

At the present time, an unusual opportunity for such a study is available to the Veterans Administration in the large groups of veterans of World War II who have been discharged from the armed forces because of cardiovascular disease. This source material is of potential value for the following reasons. First, there is available a select group of patients of military age who one or two years previ-

ously were considered physically acceptable for active military service. Second, in most cases the disease was carefully observed at its inception or evaluated during its development in military service, and the patients, as beneficiaries of the Veterans Administration, will be followed through the course of the disease to its termination. Third, the medical data available for analyses are adequate, since they include induction medical examinations, medical records of hospitalization during military service and Veterans Administration medical examinations made in outpatient departments or during periods of hospitalization following separation from military service. Lastly, these veterans live in all sections of the United States.

The present study was restricted to veterans with service-connected cardiovascular disabilities incurred in or aggravated by military service on or after December 7, 1941, who were on the Veterans Administration pension rolls up to June 30, 1944. These patients, the majority of whom have not been treated in hospitals of the Veterans Administration, comprised the largest group of cardiovascular cases among World War II veterans available for analysis.

There are three other groups of veterans with circulatory abnormalities whose cases are not included in this report and are the subjects of papers now in preparation. The first group comprises vet-

\*From the Cardiovascular Research Unit, Veterans Administration Facility.

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‡Chief, Cardiovascular Research Unit, Veterans Administration Hospital.  
§Medical statistician Cardiovascular Research Unit Veterans Administration Hospital.

erans whose disability rating claims were disallowed and who do not receive pensions and are considered as non-service-connected. In most of these cases, the cardiovascular disability was considered to have existed prior to induction and not to have been aggravated by military service. The second group is composed of patients, whether or not service-connected, who have received hospital care from the Veterans Administration. The third group includes reserve officers receiving retirement pay for cardiovascular disabilities.

The cardiovascular diagnoses used as a basis for this study were obtained from the reports of the disability boards of the Veterans Administration.

recorded. An accurate racial classification was made in 18,148 patients (Table 2). Of these, 16,065 (80.8 per cent) were Whites, 1,987 (10 per cent) were Negroes, and 96 (0.5 per cent) were of other races. In the 1,722 remaining cases, the racial factor was not clearly stated.

There were 19,789 men and 81 women.

## DIAGNOSES

### Valvular Heart Disease

The diagnosis of valvular heart disease with no etiologic factor designated was the most frequent one, being made in 5,774 cases (29.1 per cent). The ages of these patients ranged from seventeen to

TABLE 1 Distribution of Cases according to Diagnosis and Age

DIAGNOSIS	AGE (YEARS)											NOT STATED	TOTAL NO OF CASES	AVER- AGE AGE yr	AGE RANGE yr
	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69				
Valvular heart disease	262	2,568	1,439	773	521	124	50	3	2	1	0	31	5,774	26.4	17-60
Rheumatic fever	123	1,551	719	314	181	55	21	1	2	1	0	13	2,981	25.6	18-63
Hypertension	28	560	682	641	668	198	129	18	6	1	0	14	2,945	31.5	19-61
Peripheral vascular lesions	13	468	641	593	553	171	103	13	3	0	0	5	2,563	31.4	18-57
Arteriosclerosis	5	124	153	236	410	300	355	101	36	7	1	5	1,733	38.8	19-65
Neurocirculatory asthenia	13	360	335	247	248	33	10	1	1	0	0	7	1,255	29.1	19-57
Miscellaneous diseases	19	220	178	130	167	77	58	9	3	0	1	3	865	31.1	18-65
Nonvalvular heart disease (etiology unknown)	43	504	353	282	290	133	107	32	2	2	0	6	1,754	30.7	18-63
Totals	506	6,355	4,500	3,216	3,038	1,091	833	178	55	12	2	84	19,870	29.5	
Percentages	2.55	31.98	22.65	16.19	15.29	5.49	4.19	0.89	0.28	0.06	0.01	0.42			
Veterans on pension rolls	3,983	60,362	59,790	40,219	31,220	7,422	3,921	586	135	27	4	850	203,519	28.8	
Percentages of veterans on pension rolls	1.91	28.95	28.67	19.29	14.97	3.56	1.88	0.28	0.06	0.01	0.00	0.41			

These boards obtained the diagnoses either directly from the findings of the medical officers who had treated or observed the veterans immediately preceding their discharge from the armed forces or from subsequent physical examinations conducted by the medical officers of the Veterans Administration. Most of these examinations included detailed histories, physical examinations, roentgenograms of the chest, electrocardiograms and the routine laboratory procedures, as well as many special ones.

A preliminary survey of 19,870 World War II veterans with cardiovascular disease was undertaken to appraise some of the available material for the purpose of developing practical follow-up programs. The data obtained were analyzed from the viewpoints of age, sex and race, diagnosis and geographical distribution, and the trends revealed were considered of sufficient interest to report at this time.

### AGE, RACE AND SEX DISTRIBUTION

The ages ranged from seventeen to sixty-five years, with an average of 29.5 years (Table 1). Eleven thousand, three hundred and sixty-one patients (57.2 per cent) were under thirty years of age, 6,254 (31.5 per cent) were between thirty and thirty-nine and 2,171 (10.9 per cent) were forty years of age or older. In 84 cases the age was not

recorded. An accurate racial classification was made in 18,148 patients (Table 2). Of these, 16,065 (80.8 per cent) were Whites, 1,987 (10 per cent) were Negroes, and 96 (0.5 per cent) were of other races. In the 1,722 remaining cases, the racial factor was not clearly stated.

There were 19,789 men and 81 women. The diagnosis of valvular heart disease with no etiologic factor designated was the most frequent one, being made in 5,774 cases (29.1 per cent). The ages of these patients ranged from seventeen to

TABLE 2 Distribution of Cases according to Race and Sex

RACE	MEN		WOMEN		TOTALS	
	NO OF CASES	PER- CENTAGE	NO OF CASES	PER- CENTAGE	NO OF CASES	PER- CENTAGE
Whites	15,994	80.8	71	87.7	16,065	80.8
Negroes	1,982	10.0	5	6.2	1,987	10.0
Others	95	0.5	1	1.2	96	0.5
Race not reported	1,718	8.7	4	4.9	1,722	8.7
Totals	19,789		81		19,870	
Percentages		99.6		0.4		

1373. Involvement of the aortic valve alone was reported in 1,029 cases, the predominating lesion was diagnosed as aortic insufficiency in 859, and as aortic stenosis in 170. Combined aortic-valve and mitral-valve lesions, including various combinations of involvement, were diagnosed in 971 cases. The diagnosis of chronic endocarditis without reference to the valves involved was made in 120 cases, and tricuspid-valve and pulmonic-valve lesions were each diagnosed in 4 cases.

### *Rheumatic Fever*

Rheumatic fever was diagnosed in 2981 cases (15 per cent). The average age was 25.6 years, the lowest average encountered in any of the groups. Two thousand, three hundred and ninety-three patients (80.0 per cent) were under thirty years of age, and 2888 (96.8 per cent) were under forty.

Rheumatic fever without any recognized or diagnosed myocardial or valvular residuals occurred in 813 cases (27.4 per cent), valvular disease in 1853 cases (62.1 per cent), and rheumatic myocarditis or pericarditis in 315 (10.5 per cent).

The distribution of lesions among the 1853 cases of valvular disease was as follows: mitral lesions alone, 1423 cases, aortic and mitral lesions combined, 197 cases, aortic lesions alone, 150 cases, and valvular disease with the involved valves not identified, 83 cases. Mitral insufficiency was diagnosed as the main valvular abnormality in 1175 cases, and mitral stenosis, with or without insufficiency, in 248 cases. Among the lesions of the aortic valve alone, the main anatomic lesion was aortic insufficiency in 128 cases and aortic stenosis in 22.

### *Hypertension*

Hypertension was considered to be the etiologic factor responsible for the main disability of 2945 patients (14.8 per cent). Essential hypertension and hypertension with an associated cardiac disease, with or without the additional factor of coronary arteriosclerosis, are included in this category. The average age of all of the patients in this classification was 31.5 years, with a range of nineteen to sixty-one years. The large number of young people affected is noteworthy. One thousand, two hundred and seventy patients (43.1 per cent) were twenty-nine years of age or younger, and 1309 (44.4 per cent) were between thirty and thirty-nine.

### *Peripheral Vascular Lesions*

Peripheral vascular disease other than arteriosclerosis was found in 2563 cases (12.9 per cent). Six clinical entities were included in this group, with an over-all average age of 31.4 years and an age range of eighteen to fifty-seven years. Varicose veins, thrombophlebitis and chronic phlebitis accounted for 2304 (89.9 per cent) of the peripheral vascular lesions. The remaining 259 cases were distributed as follows: thromboangitis obliterans, 127 cases, Raynaud's disease, 108 cases, and arteriovenous fistula, 24 cases.

### *Arteriosclerosis*

Arteriosclerosis was considered to be the etiologic factor in 1733 cases (8.7 per cent). As was expected, the average age (38.8 years) was the highest in any group studied, with a range of nineteen to sixty-five years. Nine hundred and ninety-one (57.2 per cent) of the patients were considered as having coronary arteriosclerotic heart disease and revealed

an average age of 39.9 years, as compared to 37.8 years in the 742 cases diagnosed as arteriosclerosis without any definite statement concerning cardiac involvement.

The most interesting feature in this group was the large number of young men affected and the high incidence of coronary-artery occlusion. Of the 991 patients with coronary arteriosclerotic heart disease, 491 (49.5 per cent) were under forty years of age, 389 were between thirty and thirty-nine, and 235 were under thirty-five. Three hundred and fifty-seven patients (36 per cent) were diagnosed as having coronary-artery occlusion or myocardial infarction. Of these, 236 were under forty years of age and 177 were in the fourth decade, with 137 under thirty-five.

### *Neurocirculatory Asthenia*

Neurocirculatory asthenia was diagnosed in 1255 cases (6.3 per cent). The average age was 29.1 years, and the range was nineteen to fifty-seven years. The majority of cases were in young men, with 708 (56.4 per cent) under thirty years of age and 1203 (95.8 per cent) under forty. Many cases were undoubtedly lost sight of because this syndrome was considered or diagnosed as a part of other clinical entities.

### *Miscellaneous Diseases*

Eight diseases of the heart and blood vessels were grouped under a single classification. These affected 865 patients, whose average age was 31.1 years, with a range of eighteen to sixty-five years. This category was composed as follows: arrhythmias, 397 cases, angina pectoris, 200 cases, cerebral vascular lesions, 128 cases, pericarditis, with or without effusion, 69 cases, lesions of the aorta, 31 cases, congenital heart disease, 26 cases, acute myocarditis, 13 cases, and periarteritis nodosa, 1 case.

The etiology of the cases of arrhythmia and pericarditis was either not given or did not allow of segregation into other classifications. In the 200 cases of angina pectoris there was no mention of any associated etiologic or anatomic diagnosis. It is noteworthy that the age distribution of this small subgroup closely paralleled that of the larger arteriosclerotic group. The 128 patients with cerebrovascular lesions showed an average age of 31.5 years, with a range of nineteen to fifty-one years. There were three types of these lesions in which no etiologic factors were designated—namely, cerebral hemorrhage, 72 cases, cerebral thrombosis, 40 cases, and cerebral embolism, 16 cases. The 31 cases of aortic lesions without a definite etiologic agent were diagnosed as either aortic dilatation or aortic aneurysm. The 26 cases of congenital heart disease were considered to have been aggravated by military service. The diagnoses were as follows: patent ductus arteriosus, 7 cases, coarctation of

the aorta, 6 cases, interauricular septal defect, 2 cases, and unclassified congenital heart disease, 11 cases. The etiology was determined in all 13 cases of acute myocarditis, of which 3 were considered as due to direct trauma and 10 as secondary to identified severe infectious processes.

### *Nonvalvular Heart Disease of Unknown Etiology*

In 1754 cases (8.8 per cent), nonvalvular cardiac damage was diagnosed without reference to the etiologic factor. Chronic myocarditis, myocardial damage and cardiac degeneration were the conditions most frequently diagnosed, occurring in 1714 cases. Cardiac hypertrophy was diagnosed in 38 cases, and cardiac dilatation in 2 cases. The average age in this group was 30.7 years, with a range of eighteen to sixty-three years.

### GEOGRAPHICAL DISTRIBUTION

An analysis was made of the geographical distribution — by residence — of patients with cardiovascular disabilities, for the sole purpose of evaluating on a regional basis the follow-up potentialities of each of the discussed classifications (Table 3).

TABLE 3 *Distribution of Cases according to Diagnosis and Residence*

	NEW ENGLAND		MID-ATLANTIC		SOUTHERN		MID WESTERN		WESTERN		UNKNOWN OR OUTSIDE U S A		TOTAL	
	NO OF CASES	PER-CENTAGES	NO OF CASES	PER-CENTAGES	NO OF CASES	PER-CENTAGES	NO OF CASES	PER-CENTAGES	NO OF CASES	PER-CENTAGES	NO OF CASES	PER-CENTAGES	NO OF CASES	PER-CENTAGES
Valvular heart disease	451	7.8	1,491	25.8	1,205	20.9	1,908	33.1	704	12.2	15	0.2	5,774	29.1
Rheumatic fever	213	7.2	578	19.4	660	22.1	985	33.0	542	18.2	3	0.1	2,981	15.0
Hypertension	135	4.6	733	24.9	875	29.7	950	32.2	250	8.5	2	0.1	2,945	14.8
Peripheral vascular lesions	204	8.0	617	24.1	601	23.4	844	32.9	292	11.4	5	0.2	2,563	12.9
Arteriosclerosis	122	7.0	493	28.5	444	25.6	432	24.9	232	13.4	10	0.6	1,733	8.7
Neurocirculatory asthenia	53	4.2	286	22.8	352	28.1	464	37.0	97	7.7	3	0.2	1,255	6.3
Miscellaneous diseases	46	5.3	207	23.9	213	24.6	294	34.0	103	12.0	2	0.2	865	4.4
Nonvalvular heart disease (etiology unknown)	92	5.3	437	24.9	505	28.8	489	27.9	226	12.9	5	0.3	1,754	8.8
Totals	1,316		4,842		4,855		6,366		2,446		45		19,870	
Percentages		6.6		24.4		24.4		32.1		12.3		0.2		
Veterans on pension rolls	6,758		57,463		55,624		64,963		22,799		912		208,519	
Percentages of veterans on pension rolls		3.2		27.6		26.7		31.2		10.9		0.4		
Percentages of population (U S 1940 census)		6.4		23.0		27.4		32.7		10.5				

A fairly close agreement on a percentile basis was noted between the total series of cardiovascular cases and almost all its component groups, with the total population taken as that of the 1940 national census. It must be emphasized that this distribution refers only to the home residence in June, 1944, and in no way indicates the location of the origin or development of the various disease entities.

### DISCUSSION

The grouping of the various cardiovascular conditions incorporated in this report was not entirely satisfactory. The classification was based on the

information listed in the diagnoses used during the consideration of the veteran's first disability rating claim and were obtained from several sources, that is, the Army, the Navy and the Veterans Administration, each of which employed a different nomenclature. This made difficult the arrangement of such data in sharply delineated groups on the bases of etiologic or anatomical findings.

A more precise classification will be possible when the diagnoses are based on a uniform system of criteria and nomenclature. In the groups in which the etiology was not stated, many of the cases will be more appropriately designated. In the large group now considered as that of valvular heart disease, many cases will be reclassified as those of rheumatic heart disease. Obviously, practically all the cases of mitral stenosis and many of the cases in which the diagnosis was limited to aortic valvular disease and combined aortic and mitral valvular disease could be placed in the rheumatic group, this was not done in this survey unless the etiologic factor was stated in the diagnosis. In the rheumatic-fever group, the cases of actual cardiac disease will be more accurately separated from those of rheu-

matic fever without recognized evidence of myocardial or valvular damage, likewise, the hypertensive cases, with or without myocardial involvement, will be segregated. In any follow-up program the patients with rheumatic fever or systemic hypertension without evidence of any cardiac involvement should be classified as having potential heart disease — a separation that, at the present time, the wide variations in the nomenclature render impossible.

Study of the geographical distribution by residence showed that the various cardiovascular conditions were widely distributed throughout the Nation. This may ultimately prove of some value in apprais-

ing the effects of residence in various sections of the country on each disease entity as these cases are followed during the ensuing years

### SUMMARY

A survey of cardiovascular disease among 19,870 veterans of World War II on the Veterans Administration pension rolls as of June 30, 1944, has been reported. All the data were obtained from the reports of the diagnoses used in the evaluation of the pension claims of veterans.

The various cardiovascular conditions were classified in eight groups, based on information available

from these diagnoses, which originated from sources employing several different nomenclatures. The numbers of cases in each group were as follows: valvular heart disease with no etiologic factor mentioned, 5774 cases; rheumatic fever, with or without cardiac involvement, 2981 cases; hypertension, 2945 cases; peripheral vascular conditions, 2563 cases; arteriosclerosis, with or without cardiac involvement, 1733 cases (including 991 cases specifically designated as coronary heart disease); neurocirculatory asthenia, 1255 cases; miscellaneous diseases of the heart and blood vessels, 865 cases; and cardiac lesions other than valvular conditions, without a recognized etiologic factor, 1754 cases.

## SYMPOSIUM ON MEDICAL SOCIOLOGY

### HEALTH-INSURANCE PLANS\*

NATHANIEL W. FAXON, M.D.†

**D**OCTORS and hospitals cannot maintain a policy of isolationism in modern society any more than can governments and countries in the present economic world. The study of the interdependent relations that result is called "medical sociology." Today we are to explore some of the problems of medical sociology involving hospitals, but we shall soon discover that there are no watertight compartments in medical sociology, and that a study of hospital problems immediately involves doctors, patients and prospective patients.

The subject of this lecture is clear in its intent, as is the main objective — namely, better medical care at costs that can be borne. There is disagreement, however, as regards means.

Let us avoid in this connection such terms as "socialized medicine," "regimentation," "totalitarian control," "rugged individualism," "medical trust" and similar catch phrases, and stick to terms that will be enlightening without developing heated controversy.

### THE PRESENT SITUATION

As a foundation for the consideration of this subject, it will be well to review the present situation regarding physicians, hospitals, insurance and federal or state agencies dealing with health and sickness.

Physicians are licensed by state boards to practice medicine, either individually or in groups. They may or may not be on hospital staffs. They may be on a salary basis in a medical school, hos-

pital or industry or in a federal or state department.

Hospitals are divided into governmental hospitals — federal, state, county and city — supported by taxation, voluntary — charitable or non-profit — hospitals supported in other ways than taxation, proprietary or private hospitals intended to be profit-making, and lastly, hospitals supported by industrial companies for the benefit of their employees. All but a few of the mental, tuberculous and chronic patients are cared for in state hospitals. Ex-servicemen in these classes are cared for in federal veterans' hospitals. There are many municipal general hospitals, and most communicable-disease hospitals are tax-supported.

There are also the United States Public Health Service and the various state departments of health, with whose duties everyone is familiar. The federal government conducts the equivalent of industrial accident insurance for federal employees. There are the Children's Bureau and its Emergency Maternity and Infant Care Program, as well as the Old-Age Insurance and Care of Crippled Children programs of the Federal Security Agency. In Massachusetts there are the Industrial Accident Board, the welfare departments of state, cities and towns, the Division of the Blind and no doubt many others.

It is thus evident that there is already an extremely wide participation by government in medical affairs and that a large amount of tax funds goes into these activities. It seems axiomatic that any further extension should be built on this framework, complementing and supplementing rather than replacing existing agencies. This is important to keep in mind.

\*This is the third of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March 1945, they were sponsored by the Department of Preventive Medicine and were primarily intended for third year students.

†Director, Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary.

Most insurance companies pay a cash indemnity to the subscriber to cover hospital costs or medical fees. The Blue Cross supplies a service payment by paying hospital charges. There is a great difference between these. The cash indemnity may or may not cover hospital charges, and in the latter case the balance of cost must be borne by the patient or the hospital. Moreover, the indemnity is paid to the individual, who may or may not pay the hospital. Service payment does cover the hospital charges up to the period of hospitalization granted, which is thirty days, with a 50 per cent reduction for ninety days more. This payment, of course, covers all but the most unusual cases. It is made to the hospital.

#### BASIC STATEMENTS

All consideration of this subject should begin with a reading of the report of the Committee on the Costs of Medical Care, published in 1932, which presents the results of careful research and considered opinions based on them. Since the issuance of this report many other studies have been made, and out of all these have come the following generally accepted facts.

There are four groups of persons in the population. The first group includes the rich or well-to-do, who have ample resources to meet the costs of medical and hospital care, with annual incomes of \$5000 or over. They form 9.2 per cent of the population. The second group is the upper middle class, with annual incomes of \$2000 to \$5000, forming 35.2 per cent of the population. Voluntary Blue Cross plans have appealed to this group. The third group is that of the wage earners, with annual incomes from \$1000 to \$2000, forming 41.0 per cent of the population. The fourth group comprises the indigent, persons with annual incomes below \$1000, forming 14.0 per cent of the population.

Estimates of the cost of medical care vary, but it is somewhere between \$25.30 and \$66.97 for the provision of adequate medical care — that is, house, office and hospital care by physician and nurse, hospital care and to some extent dental care.

It is generally accepted that if people would pay into an insurance plan all the money they now pay to doctors, hospitals and nurses, together with what they spend on medicines, including patent medicines, full medical hospital and nursing care could be provided without further expenditure. But no one is naïve enough to believe that things will work out in this way.

On certain points there is general agreement. First, medical care is costly. Sickness is unpredictable, regarding both the persons affected and its frequency and length. There is need of some method to spread this cost, either by insurance or by taxation. Second, hospitals and doctors are concentrated in cities and scarce in rural areas. There is need to even this imbalance. Hospitals should be

built in isolated places and doctors subsidized to practice there. Third, more medical care would be advantageous, especially in the field of preventive medicine. The poor get less care than they need, and the rich probably pay more for such care than they should. Fourth, medical education must be carried beyond graduation from medical school. Lastly, research must be supported.

#### PRESENT INSURANCE PLANS

Until recently, sickness has been regarded as something to be handled when it occurs. This attitude has been attacked from the medical side through the development of preventive medicine, and from the social side through the development of prepayment plans or the application of the insurance principle.

#### *Voluntary Insurance*

*Commercial insurance companies.* Insurance companies have for a long time sold accident insurance and, in a small way, sickness insurance with cash indemnity, the latter being handled as a sideline of life insurance. Now, however, since insurance against the costs of medical and hospital care are arousing interest, many insurance companies are offering policies similar to those of the Blue Cross and Blue Shield, except for the fact that they provide for cash indemnity.

The Workmen's Compensation Act is a form of insurance against industrial accidents and sickness.

*The Blue Cross.* The Blue Cross was developed to provide a means of spreading the cost of hospitalized illness through prepayment on the insurance principle. It began in Dallas, Texas, in 1932 in a limited way to provide care in the University Hospital for teachers in Baylor University, and rapidly spread to other sections of the population of that city. With the interest and support of the American Hospital Association, certain principles of operation were developed and published. There are now eighty plans in thirty-eight states, with over 16,000,000 subscribers.

The Massachusetts Blue Cross, started five years ago, has 1,000,000 subscribers. The plan is based on actuarial figures showing that of every 10 persons one is hospitalized each year for a period of slightly less than ten days — (just under eight for men and just over eight for women). It is thus estimated that for every 1000 persons insured there will be about one thousand days of hospital care.

The success of the Blue Cross is due to the fact that it meets a need in a practical way. It is a non-profit organization and is safeguarded by coming under the direction of the State Commissioner of Insurance. The governing body is composed of sixteen directors, a majority of whom must be trustees, directors or staff members of hospitals, the remainder being representatives of the Massachusetts Medical

Society and selected representatives of industries whose employees are insured

It is preferable to insure under the group method, since thereby no physical examination is necessary because the undesirable risks are automatically cancelled. Sixty per cent of the employees of any group of 50 or more must be enrolled, below this number a higher percentage must participate. Individual subscribers can be enrolled by submitting to a physical examination, for which they pay. The cost of membership is \$10.00 a year for single persons, \$19.80 for a husband and wife and \$24.00 for a family, regardless of the number of children.

The Blue Cross collects money from its subscribers, issues certificates of membership, makes contracts with hospitals and pays the hospital charges of its members. The hospital makes to the Blue Cross exactly the same charges, with a few exceptions, that it would render to an ordinary patient, but with a maximum daily charge of \$6 for thirty days. As previously stated, if hospitalization is continued beyond this period, the Blue Cross pays 50 per cent of the hospital charges for ninety additional days.

Blue Cross plans are quite satisfactory so far as hospitalization goes, since they are inclusive, economical and widely available.

### *The Blue Shield*

The success of hospital-insurance plans has led to a demand for similar insurance to cover professional fees for hospital illnesses. To meet this demand, organizations have been set up and sponsored by state and other medical groups. They were started later than the Blue Cross but are now operating in thirteen states, containing 50 per cent of the population of the United States. The largest unit is in Michigan.

The Blue Shield, the name applied to the corporation founded by the Massachusetts Medical Society, was formed in June, 1943. It insures single persons with annual incomes up to \$2000 and families with incomes up to \$2500 and pays their doctors' fees for surgical or obstetric care in hospitals. The doctors participating in this plan accept a standard fee for operations and obstetric care. About 88,000 persons are now enrolled. The cost of membership is \$10.00 a year for single persons, \$19.80 for a husband and wife, and \$24.00 for a family.

Blue Shield plans should and will be expanded, as rapidly as can be safely done through the gathering of actuarial experience, to include medical care and a wider range of incomes by the grading of fees.

Having seen how desirable it is to use prepayment plans for the more costly and financially crippling hospital illnesses, people are now demanding similar protection against all medical care and all sickness. Here comes the rub, for there is a wide divergence of opinion concerning what this pro-

tection will cost, estimates varying all the way from \$26.00 to \$66.00 a year per person.

### *Ross-Loos Medical Group*

The Ross-Loos Medical Group, of Los Angeles, a partnership of physicians, gives 27,000 persons complete medical care in homes and in the clinic and permits ninety days' hospitalization for \$30.00 a year. Obstetric and dental care and the care of venereal disease are not included. This group has had a stormy career, being opposed by the American Medical Association and suffering from financial growing pains because its actuarial figures were at first faulty.

### *Kaiser Permanente Foundation*

The Permanente Foundation, of Henry Kaiser, an industrial-insurance plan that provides medical care in the company hospital at \$6.00 a year for 62,000 employees, has recently attracted attention. The foundation plans to take families of three or more for \$7.50 a month, — \$90.00 a year, — or \$30.00 per person, which is a reasonable sum for complete medical care.

### *The Group Health Association*

The Group Health Association, in Washington, D. C., has also been much in evidence because of the suit brought by the United States Government against the American Medical Association.

### *Compulsory Insurance*

Comprehensive compulsory health insurance by governmental legislation was first advanced as far back as 1916. The Workmen's Compensation Act resulted, but interest in health insurance lapsed and was not resumed until 1932, when the Social Security Bill was proposed. The medical plans therein set forth were pigeonholed, but the old-age pension and unemployment features of the bill were enacted. Ever since that time the health-insurance proposals have been revived from time to time, and these have recently been given prominence by the introduction of the Wagner-Murray-Dingell Bill. The American Medical Association has opposed all such legislation. Scrutiny of this bill has revealed many defects. Many groups have studied it, and some have made helpful suggestions concerning how such legislation can be safeguarded.

The recommendations made by a group known as the Health Program Conference are the most complete and rational of those proposed. They were published as "The Principles of a Nationwide Health Program" in November, 1944, by the Committee on Research in Medical Economics of New York, a foundation-supported organization. This program is too long to describe in detail, but its ten principles give some idea of its character. These are as follows: comprehensive coverage and service, spreading of costs, distribution of facilities according to community health requirements, encouragement of group medical practice, with hospital and

professional health centers, determination of policy through the participation of those who receive and of those who furnish service, responsibility of the medical profession for strictly medical activities, freedom of choice for physicians and patients, adequate payment of physicians and hospitals by methods that encourage quality and promote economy of service, a national system, and local administration of services under national standards.

Certain points deserve emphasis. A national system has obvious advantages. One of these is collection of payment through wage deductions, which gives benefits regardless of place of residence. Local administration is necessary because federal administration cannot adjust itself to local conditions, and because decentralization is mandatory. Control of policy should be in the hands of physicians and subscribers, not in those of a government bureau head such as the Surgeon General of the United States Public Health Service. Distinction between administrative and medical responsibilities is required, for physicians must be charged with the latter only.

The costs are to be met by contributions amounting to 12 per cent of all wages up to \$3000 a year, 6 per cent to be paid by employers and 6 per cent by employees. This means that a worker earning \$2000 will have to pay \$120. For this sum he and his dependents will receive full medical care in the home, the doctor's office and the hospital.

\* \* \*

The proposals for health insurance comprise three views, supported by as many different groups.

The American Medical Association opposes any national legislation, insists on individualism and advocates the extension of Blue Shield and Blue Cross plans.

The American Hospital Association proposes grants-in-aid to the states for all necessary hospital and medical care for recipients of public assistance, which strikes at the heart of an important economic problem of sickness, and the promotion of Blue Cross plans. Health and health service, it is held, are extremely personal matters. The best results are obtained when patients co-operate actively in a program of prevention and treatment that includes the payment of costs. When such participation is voluntary, a certain amount of discipline of the worker, the hospital and the doctor is involved. This condition would not exist to the same extent under a taxation plan. The Blue Cross is essentially a form of public service, yet it accomplishes its aim without public compulsion. Federal employees cannot authorize deductions for the Blue Cross. It would be well for the Government to allow this. The American Hospital Association also favors grants to states for the erection of hospitals where needed when the community cannot afford to provide them, extension and expansion of Blue Shield activities

and the development of group medicine in clinics and hospitals.

The proponents of compulsory plans hold that, even granted that voluntary plans are growing, they are too slow and will never include all those who should be protected, that there will be wide differences in coverage and benefits and that a voluntary system is spotty and not inclusive. These persons believe that it will be a simple matter to extend the mechanism of the present Social Security Act to include comprehensive medical care for all wage earners throughout the country, but that this can be successfully accomplished only through compulsory legislation.

The following defects of compulsory insurance have been pointed out. People dislike compulsion. They also dislike federal control. (This can be partially overcome by decentralization through the local administration of distribution of benefits.) They fear bureaucratic development and control of doctors and hospitals and dictation as to medical care. They fear political intrusion. Lastly, they are perturbed by the increasing number of pay deductions for taxes. This plan will immediately increase these by 6 per cent, and ultimately each wage earner will pay 4 per cent more, a total of 10 per cent, which will bring the total tax payment to 35 to 40 per cent.

The present situation reduces itself to the question whether people wish to have insurance against sickness develop gradually through the extension and development of voluntary plans, such as those of the Blue Cross and the Blue Shield, which they can join if they so desire, or prefer to have federal legislation that will set up a comprehensive compulsory health-insurance plan covering all wage earners, with eventual payroll deductions of 10 per cent. The chief advantage of the first method is that, although slow, it is evolutionary and voluntary, that of the second method is that it will be immediate and comprehensive. The main disadvantage of the compulsory method is that it cannot help being cumbersome, with the inherent faults of bureaucratic control and, ultimately if not immediately, the intrusion of politics.

The object of the present lecture is not to settle this question, but to present the facts of the situation for study and evaluation.

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Society and selected representatives of industries whose employees are insured

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was given intramuscularly every two hours. The nonprotein nitrogen rose to 160 mg per 100 cc. Large hemorrhagic patches and purpuric spots appeared over the entire body. Respiratory distress became pronounced, with hemoptysis. Rales were heard in both lungs. The pulse became slow, and the respirations more difficult. The patient expired one month after admission.

### DIFFERENTIAL DIAGNOSIS

DR. CHARLES L. SHORT: In summary, this is a patient with a definite past history of treated syphilis, and a positive Hinton test eight years before entry. These facts immediately introduce a disturbing element, but one that I am willing to eliminate as a primary factor in the terminal illness, provided that syphilis is not the etiology of the cardiac murmurs and valvular disease. The quality of the murmurs is not described but evidently there was a loud systolic murmur as well as a diastolic murmur at the aortic area, which was transmitted to the neck. We should like to know whether there was a thrill and whether aortic stenosis might have been diagnosed, thus suggesting rheumatic heart disease.

Perhaps the x-ray films will show whether there was dilatation of the aorta.

DR. CLAYTON H. HALE: The aorta is not remarkable in this film. It does not appear widened but there is slight tortuosity. The heart itself is only slightly enlarged, without characteristic configuration. This plain abdominal film shows the large spleen and the calcified nodes.

DR. SHORT: Can you see the liver?

DR. HALE: The liver edge does not show up particularly well. There is only slight if any enlargement of the liver, however.

DR. SHORT: A lot of skeletal films were taken. I suppose that we can assume that they were negative.

DR. HALE: That is correct.

DR. SHORT: And the calcified area is probably due to old tuberculous lymph nodes?

DR. HALE: I should think so.

DR. SHORT: The aortic lesion was probably nonsyphilitic. This is also favored by the negative Hinton test at the time of admission and the lack of preceding symptoms suggesting syphilitic aortitis. The skeletal x-ray films were probably taken with a view to the diagnosis of multiple myeloma, although, of course, they might have been taken with any form of malignant disease, probably metastatic, in mind. The diagnosis of multiple myeloma is a possibility, but the negative x-ray films, the lack of Bence-Jones proteinuria, the low serum protein and the absence of anything suggesting bone pain until late in the disease make it unlikely.

To go on with the summary, the patient had indefinite constitutional symptoms five months before the purpuric spots appeared. He contracted what

was probably an intercurrent upper respiratory infection, and this may have been a precipitating factor in the severe epistaxis that brought him to the hospital. On examination he had the murmurs I have mentioned, purpuric spots and a few somewhat enlarged lymph nodes, one of which was biopsied and found to show only chronic inflammation. He had a palpable, possibly enlarged liver and an enlarged spleen. In addition, he had a fever of 102°F. On the laboratory side he had a moderate normochromic anemia and a low white-cell count, with the neutrophils showing a shift to the left, suggesting infection. He had normal renal function as measured by the urinary findings and the nonprotein nitrogen. Studies regarding the purpura disclosed no significant increase in the prothrombin time, an increased bleeding time and a definitely increased clotting time.

The x-ray films that we have seen are not helpful. The patient had a downhill course, with chills and a spiking fever to 103°F, the development of ascites and finally either cardiac failure or bronchopneumonia, or perhaps both. He continued to bleed and he had a terminal rise in the nonprotein nitrogen without any mention of what the urinary findings were at that time.

On reading this case over rapidly my first impression, which is sometimes but not always the best one, was that he had severe liver disease, presumably cirrhosis. The bleeding, although the prothrombin time was not definitely increased, the low white-cell count, the depressed serum albumin, the ascites, the palpable liver and the splenomegaly all seem to fit in with this diagnosis. After reading more carefully, however, I found the sentence stating that he had a fever of 103°F, with chills. This made me pause, as well as the absence of jaundice in a patient with as much bleeding and who was as sick as this. I believe, and Dr. Jones may correct me on this, that a fever of this type and duration is incompatible with the diagnosis of hepatic cirrhosis in the absence of a complicating infection. I accordingly decided against that diagnosis.

The primary or idiopathic form of purpura must, of course, be considered. As for the thrombopenic variety, the bleeding time was only slightly, if at all, increased compared to the clotting time. The clot retraction was presumably normal, and the platelets were said to be decreased, rather than absent or nearly absent. In regard to the type of idiopathic purpura that is not associated with platelet depression, cases as severe as this have been described with fatal termination, but the diagnosis is questionable. Probably many of them were cases of disseminated lupus erythematosus. And this brings up the possibility of disseminated lupus, which may be associated with severe purpura, in addition, I remember one patient who also had ascites. I do not believe, however, that there is enough positive evidence to consider that diagnosis any further.

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT.

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 32031

#### PRESENTATION OF CASE

A fifty-one-year-old man entered the hospital complaining of severe nosebleed.

Six months before admission he first noted undue fatigability, anorexia and malaise. These symptoms increased during the following months. He was forced to quit his occupation of messenger and did a number of odd jobs, including painting. One month before admission, numerous small, red, non-elevated, nonitching, painless spots appeared over the lower legs and feet. An individual spot would persist for a time and disappear. New lesions would then develop. Three weeks before admission he was exposed to rain and cold and contracted a severe cold. His nose was obstructed, and a dry hacking cough developed. Each morning he awoke with a severe frontal headache, relieved by clearing the nasal passages. The material produced on blowing the nose resembled clots of blood, but there was no actual bleeding. He had had cramping pains in the calves and thighs, relieved by exercise. The evening before admission severe hemorrhage occurred from the right nostril and lasted for six hours. There was no bleeding from the gums. During the previous six months he had lost 16 pounds of weight.

There was no history of rheumatic or scarlet fever. Twenty-five years before admission he had been treated at this hospital for syphilis over a period of three years. Eight years before admission, the blood Hinton test was positive.

Physical examination revealed the patient to be well developed and thin, he appeared fatigued and uncomfortable. The pupils were normal. There was no epistaxis. The skin was extremely dry, with scaling over the lateral aspect of the right leg. One posterior cervical node was palpable, and one in the right axilla. A Grade III systolic and a diastolic murmur were heard over the aortic area and were transmitted upward along the great vessels. A Grade II systolic murmur was heard at the apex. The lungs were clear except for inspiratory rales at the right base. The liver was palpable three finger-breadths below the right costal margin and was

firm and nontender. The spleen was firm, nontender and palpable 6 cm. below the left costal margin, 1 cm. to the left of the midline. There were numerous purpuric spots, measuring 1 to 3 mm. in diameter, over both legs up to the groin. A tourniquet test was positive.

The temperature was 102°F, the pulse 90, and the respirations 30. The blood pressure was 130 systolic, 70 diastolic.

The red-cell count was 3,700,000, with 10.5 gm. of hemoglobin. The white-cell count was 4600, with 70 per cent neutrophils, 18 per cent of which were immature. The platelets were decreased. The bleeding time was 4½ minutes, and the clotting time 45 minutes. The urine was cloudy, amber and acid, with a specific gravity of 1.022. It contained no albumin, casts or cells. The nonprotein nitrogen was 30 mg. per 100 cc. and the total serum protein 4.8 gm., with 2.8 gm. of albumin and 2.0 gm. of globulin. The prothrombin time was 21 seconds (normal, 15 to 18 seconds). The serum chloride was 98 milliequiv. per liter. A blood Hinton test was negative. Four blood cultures were negative.

An x-ray film of the chest revealed clear lung fields and a normal-sized heart. The spleen was enlarged. There were no abnormal soft masses in the abdomen. There were several calcified areas in the right upper quadrant. The skull, lumbar spine, pelvis, humeri and knees were negative.

The white-cell count varied from 2400 soon after admission to 12,600 later in the course of his disease. The temperature spiked from 99 to 103°F, with chills.

Nine days after admission the patient complained of sharp pain in the lumbar region, more marked on the right than on the left, which was aggravated by motion. Slight tenderness was elicited over the right costovertebral angle, but according to the patient the pain was more medial. X-ray examination showed no fractured rib. The abdomen was not tense, but distended with gas and tympanic. Evidence of free fluid was present. Peristalsis was high pitched. A flat film of the abdomen revealed a considerable amount of gas in the colon and less in the lower loops of the small intestine. Repeated blood and plasma transfusions resulted in an elevation of the plasma protein to 6.4 gm. Two days later more petechiae were noted over the legs. Biopsy of an axillary lymph node revealed chronic inflammation. The ascites increased. Paracentesis yielded 2500 cc. of slightly bloody fluid, with a specific gravity of 1.008. It contained 3 lymphocytes per cubic millimeter, but no bacteria or tumor cells were seen on smear. The patient was much relieved by the procedure, but the fluid again rapidly accumulated. Gaseous distention and lumbar pain persisted. Paroxysmal sinus tachycardia appeared and the patient became dyspneic. He coughed up thick pinkish-white sputum. Shifting dullness was found in the right chest. Penicillin (32,000 units)

ndocarditis In this picture (Fig 1) you can see the interadherence of the two cusps at the commissure. There, also, the part of the cusp not involved with bacterial endocarditis is thickened, showing the old rheumatic infection You can also see the thickening of the chordae tendineae of the aortic leaflet of the mitral valve The chordae were slightly shortened, but not enough to cause appreciable stenosis Microscopically there were small infarcts in the myocardium due to small emboli from the aortic valve These may be a real factor in the production of the cardiac failure seen in subacute

DR JONES We have seen it, but the cirrhosis is usually accompanied by real liver failure I wonder whether there was much hepatic failure

DR CASTLEMAN There may have been a little, but microscopically there was only mild cirrhosis and slight chronic passive congestion

DR RICHARDSON What about the increased clotting time? Can you answer that? He certainly had an increased clotting time and a tendency to bleed, and they were not due to platelet lack

DR CASTLEMAN Patients with bacterial endocarditis do have a tendency to bleed I am under

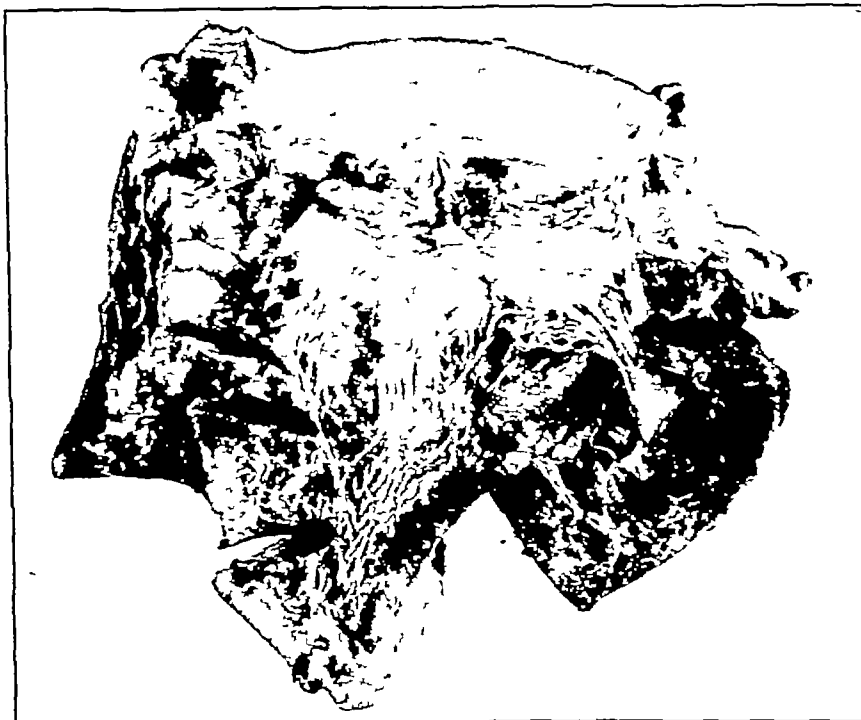


FIGURE 1 Photograph of Heart

bacterial endocarditis This man also had infarcts in both kidneys, and I suppose the pain in the back was due to one of these infarcts The spleen weighed over 400 gm and showed infarction There was a severe terminal bronchopneumonia He had a mild portal cirrhosis, which may or may not have had anything to do with the recent illness

DR RICHARDSON Why the ascites? Was it cardiac? Since he had a low protein, I should think that one could say that the liver did have something to do with it

DR CASTLEMAN It was a very mild cirrhosis, with only slight fibrosis in the portal spaces The liver had not shrunk, in fact it was larger than normal I had supposed that the anasarca was due to cardiac failure It could have been due to a combination of both factors

DR RICHARDSON The serum protein was certainly low

DR CASTLEMAN Yes, but I do not recall having seen 2 liters of fluid in each pleural cavity as a result of a low protein

the impression that some of the so-called "petechiae" seen in subacute bacterial endocarditis are not embolic but the result of capillary damage

DR BLAND That is one idea, but I have never seen it happen in the presence of such an increase of the clotting time

DR SHORT I have never heard of a case like this, with a bleeding tendency associated with an increased clotting time

DR RICHARDSON It is usually due to a toxic purpura

DR BLAND This is a disturbing case. I have looked for years for a case with this degree of heart failure and a normal-sized heart I think that other factors should be emphasized Were the veins distended?

DR COTZIAS Dr Kennedy thought that they were not distended

DR BLAND That is against heart failure

DR JONES Perhaps the anasarca was due to a low serum albumin without cirrhosis A number of cases get a low albumin due to prolonged malnutrition

In any obscure illness periarteritis nodosa sooner or later raises its head, and it must be thought of here. Purpura has been described in this disease, but again there are no characteristic manifestations to allow me to discuss this possibility further.

One must also mention lymphoma in passing, which was evidently considered, on account of the lymph-node biopsy. I think we can also pass by lymphoma, as well as leukemia, with the comment that positive evidence is wanting.

So far I have not mentioned any disease of known infectious origin except syphilis. Those in charge of this patient evidently thought of this possibility when the blood cultures were taken and when they finally began to treat him with penicillin. I think that a diagnosis of subacute bacterial endocarditis must have occurred to all of you, with the combination of a valvular lesion, chills, fever, anemia and an enlarged spleen. I say "a valvular lesion," although that has not been proved, but I think that we must assume that it was there and that the murmurs were not merely associated with a moderate anemia, which he had on admission to the hospital. Frank purpura with platelet depression is occasionally found in this disease. The points about this diagnosis are the negative blood cultures, which do not eliminate it, and the development of ascites, although the latter may have been due to cardiac failure or the low serum albumin, or to a combination of the two. The lumbar pain may be explained on the basis of renal infarcts. These or likelier the glomerulonephritis found quite often in cases of subacute bacterial endocarditis may have accounted for the terminal rise in nonprotein nitrogen. So I should like to propose as a diagnosis in this case subacute bacterial endocarditis arising from rheumatic disease of the aortic valve.

DR BENJAMIN CASTLEMAN Dr Bland, have you an opinion?

DR EDWARD F BLAND I agree with Dr Short.

DR WYMAN RICHARDSON This was indeed a puzzling case. I should like to say that, so far as the murmurs were concerned, Dr Kennedy of the House Staff in one of the later notes stated that a definite mitral murmur was heard, which led to the diagnosis of a rheumatic heart. I also put down a note saying that I could not hear this murmur. You can believe either one of us.

Another puzzling thing to me was the clotting time. It was definitely prolonged, and the tendency to bleed was not due to platelet lack. Was the sedimentation rate determined?

DR GEORGE C COTZIAS Yes, it was increased.

DR RICHARDSON If the increased clotting time was due to severe liver disease and fibrinogen lack, the sedimentation rate might have been slow, but I do not know whether that can be used as a yardstick. We did not measure the actual fibrinogen levels in the blood, which might have been interesting.

I wrote in the record as follows:

I cannot easily put this picture together. There is not sufficient evidence in the blood picture to establish a diagnosis of leukemia. The platelets, although reduced, are not low enough to produce purpura, the bleeding time is normal. He has a "toxic" purpura, possibly enhanced by prothrombin lack. The heart lesion, which I think is aortic regurgitation without definite mitral stenosis, can well be syphilitic. However, I think the most likely diagnosis is bacterial endocarditis, with superimposed liver failure, probably cirrhosis.

DR CHESTER M JONES Dr. Short raised the question of fever in relation to cirrhosis. Occasionally in cirrhosis one gets prolonged fever, usually individual spikes for two or three days. It could go to that height or higher in short spikes.

DR SHORT But not a continued fever and not with chills?

DR JONES No, continuous fever is unusual. In regard to the sedimentation rate, I think that Dr Richardson is wrong. In cirrhosis of any degree the sedimentation rate is usually greatly increased. One thing against an early type of cirrhosis is the one figure for the globulin, which was relatively low. Most advanced cases of cirrhosis tend to have normal or high globulin levels.

#### CLINICAL DIAGNOSES

Subacute bacterial endocarditis?  
Purpura (? etiology)  
Cirrhosis of liver?

#### DR SHORT'S DIAGNOSES

Subacute bacterial endocarditis  
Rheumatic valvular disease, aortic, with regurgitation  
Renal infarcts?  
Glomerulonephritis?

#### ANATOMICAL DIAGNOSES

Subacute bacterial endocarditis, aortic valve  
Rheumatic heart disease, with mitral and aortic involvement  
Myocardial infarcts, small, multiple  
Portal cirrhosis of liver, mild  
Anasarca  
Infarcts of kidneys and spleen  
Bronchopneumonia

#### PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN The autopsy showed what at first glance seemed to be severe cardiac failure. There was anasarca, with 3 or 4 liters of fluid in the abdominal cavity and 2 liters in each chest cavity, as well as peripheral edema. The heart, however, was normal in size and was involved with subacute bacterial endocarditis. There was old rheumatic heart disease, with mild involvement of the mitral valve and mild interadherence of the aortic cusps, but apparently not enough to produce cardiac hypertrophy. Superimposed on the old rheumatic aortic valve was a subacute bacterial

the spine. Six weeks before readmission, the patient noticed pain in the lower anterior portion of the left chest. It was constant, sharp and localized, and was made worse by lying down or on deep breathing. Three days before admission the pain became more severe than usual, and he had shaking chills.

On physical examination the left lower portion of the chest was dull to percussion laterally and posteriorly, with absent tactile fremitus and faint breath sounds.

The temperature was 101°F, the pulse 90, and the respirations 25.

The white-cell count was 6100, with 63 per cent neutrophils. The urine was negative. The non-protein nitrogen was 22 mg per 100 cc, and the serum protein 7.2 gm, with 4.6 gm of albumin and 2.6 gm of globulin. The serum calcium was 8.6 mg per 100 cc, the phosphorus 2.5 mg, the alkaline phosphatase 11.7 Bodansky units, and the acid phosphatase 1.2 units. The urinary calcium output was 158 mg in twenty-four hours.

An x-ray film of the chest showed that the left lower lung field was obscured by ground-glass density. There was a linear area of increased density along the left lateral chest wall. The right lung field was clear. After thoracentesis had been done, it was found that the lung markings of the left lower lobe were crowded behind the heart. The visualized bones of the dorsolumbar spine and pelvis showed no definite evidence of metastatic involvement.

One month later only a small amount of fluid was found in the left pleural cavity, chiefly posteriorly, obliterating the left costophrenic sinus. The left lower lobe was markedly decreased in size. There was slight displacement of the heart and mediastinum to the left, and considerable emphysema of the left upper lung field. The heart and the right lung were normal. Two months after admission, narrowing of the interspace between the twelfth dorsal and first lumbar vertebrae was seen. The first lumbar vertebra showed multiple areas of diminished density throughout, particularly in the anterior portion of the body. About these areas of diminished density were areas of increased density. The skull, lower legs, forearms and hands showed no bony abnormality.

Repeated thoracenteses were done, which yielded up to 1000 cc of dark-yellow, slightly hazy fluid that contained no acid-fast bacilli or tumor cells. The patient continued to complain of lumbar pain, and also of abdominal pain radiating to the flank, with tenderness. Bronchoscopy was negative. He was discharged somewhat improved.

*Sixth admission* (three months later). The pain in the lower back, hips and legs had continued, being severer on the right than on the left. There were areas of numbness on the anterior and lateral aspects of each thigh. There was no pain in the neck.

Physical examination revealed dullness to percussion over the left lung base in an area about 6 cm

wide. The breath sounds were normal. There was slight tenderness over both costovertebral angles. The left knee jerk was less active than the right. The abdominal reflex was questionably absent on the right. Over the areas of subjective numbness described above, the patient was unable to distinguish between sharp and dull.

The white-cell count was 7700, with 69 per cent neutrophils. The urine was negative. The serum calcium was 11 mg per 100 cc, the phosphorus 2.4 mg, the alkaline phosphatase 8.7 Bodansky units, and the acid phosphatase 2.4 units. A guinea pig inoculated with chest fluid obtained three months previously was killed and reported to be negative. Agglutination tests for typhoid fever and brucellosis were negative.

An x-ray film of the chest revealed no change in the appearance of the lungs. The destructive process involving the bodies of the twelfth dorsal and first lumbar vertebrae had increased, with narrowing of the disk space. At the lower portion of the body of the twelfth thoracic vertebra there was a cavity apparently containing sequestrums. There was also beginning involvement of the lower surface of the first lumbar vertebra and the disk below it.

Lumbar puncture obtained clear fluid under an initial pressure equivalent to 105 mm of water. On jugular compression the pressure rose to 350 mm and fell slowly to 130 mm in release, the final pressure was 90 mm. The total spinal-fluid protein was 47 mg per 100 cc.

An operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR OTTO E. AUFRANC. It seems that, chemically, this patient improved considerably after the adenoma of the parathyroid gland was removed. So we might eliminate that entirely from the discussion.

May we see the x-ray films?

DR CLAYTON H. HALE. This chest film shows evidence of old pleurisy on the left, and the left lower lobe is collapsed. No evidence of metastases is seen, and there is no definite tuberculous lesion in the lung fields. This film of the abdomen was part of an intravenous pyelogram and shows normal kidneys. There are hypertrophic spurs of the vertebral bodies, most marked about the second lumbar vertebra. The next films, taken in the early part of this year, show definite destruction of the twelfth thoracic vertebra, and there also appears to be narrowing of the twelfth interspace. I cannot make out a definite soft-tissue mass about this vertebra, although the psoas shadow on the right in some of the films looks a little fuller than that on the left. In the differential diagnosis one must consider a malignant neoplasm, primary or metastatic, and infection. The fact that the interspace is narrowed suggests an infectious process, even though we do not have a definite soft-tissue mass to go with it.

DR. SHORT Did he have glomerulonephritis?  
 DR. CASTLEMAN No

### CASE 32032

#### PRESENTATION OF CASE

*First admission* A forty-one-year-old man, a foundry chipper by trade, entered the hospital complaining of pain about the umbilicus, radiating to the right lower quadrant and to the right testis.

Fifteen years before admission the patient had had severe right renal colic and had passed a stone. Following this attack, he had had many other episodes of renal colic, passing stones each time.

Physical examination was negative.

The red-cell count was 4,100,000, with 75 per cent hemoglobin. The white-cell count was 9100. The urine was light amber and acid, with a specific gravity of 1.020. It gave a + test for albumin, and the sediment contained 150 red cells and an occasional white cell per high-power field. The urine was sterile on culture. The nonprotein nitrogen was 23 mg per 100 cc, and the serum protein 6.1 gm. The maximum serum calcium was 15.7 mg per 100 cc, with a phosphorus of 2.4 mg. The alkaline phosphatase was 10.7 Bodansky units. The urinary calcium output was 489 mg in twenty-four hours. A blood Hinton test was negative.

An x-ray film of the abdomen showed a 1-cm stone in the region of the right kidney pelvis. There were two minute areas of calcification in the lower pole of the left kidney. The bones were normal in density.

The patient underwent a right pyelolithotomy, from which he recovered uneventfully. The stone obtained consisted of phosphatase.

*Second admission* (one month later) The patient was readmitted to the hospital, and an adenoma of the left lower parathyroid gland, measuring 2 by 1.5 by 1.5 cm, was removed. The patient recovered without tetany. Two days after the operation, the serum calcium was 10.3 mg per 100 cc, the phosphorus 1.5 mg, and the alkaline phosphatase 7.1 Bodansky units. The Sulkowitch test for urinary calcium was negative at discharge.

*Third admission* (twenty months later) After discharge the patient felt well and passed no stones. Soon, however, he noted the gradual development of an area of hypesthesia on the anterior aspect of each thigh. Each area was small at first but then grew larger, involving the lateral aspect of the thigh as well. Five months before readmission he had a chill, and a short time later he complained of a dull, constant, nonradiating ache in the midline of the upper lumbar region, which was associated with a considerable amount of spasm of the lumbar muscles. Exertion seemed to relieve the pain somewhat, and leaning forward and to the right aggravated it. An x-ray film showed moderate scoliosis of the dorsal spine, with convexity to the right. The

lumbar spine had a mild compensatory scoliosis to the opposite side. The neural arches of the first sacral segments were not united. There were hypertrophic changes throughout the spine. Two fairly large spurs arose from the lateral margins of the body of the second lumbar vertebra. In spite of a back brace and a change to a lighter type of work, the back pain persisted, occasionally waking the patient at night. It became much worse on coughing or sneezing. The patellar and Achilles tendon reflexes were diminished. There was no Babinski sign. Since the pain had become so severe, he was admitted for further study.

There was no tenderness of the lumbar vertebrae at the site of the pain, which was especially severe when the patient straightened up after leaning over.

The serum calcium was 9.6 mg per 100 cc, the phosphorus 2.4 mg, and the alkaline phosphatase 6.8 Bodansky units. The spinal fluid was negative.

An intravenous pyelogram was negative. The bones of the lumbar spine and pelvis were slightly decalcified, and there was incomplete fusion of the laminae of the sacral segments. There were moderate degenerative changes about the bodies of the first and second lumbar vertebrae. A lateral film of the lumbar spine and stereo films of the sacroiliac joints revealed normal intervertebral-disk spaces. There was slight new-bone formation in the antero-central portion of the left sacroiliac joint. A gastrointestinal series and a barium enema were negative.

The pain persisted, with variations in intensity. The hypesthesia of the thighs also continued. Several weeks after admission the patient began to expectorate about 10 cc of blood-tinged fluid every morning. There was no cough. No bleeding point was found in the mouth or pharynx. A chest film showed normal lungs. On discharge, two months after admission, he was walking for short periods and complained infrequently of slight back pain.

*Fourth admission* (one year later) Three weeks after discharge the patient returned to the Out Patient Department, with marked increase in the back pain. X-ray treatment (600 r) was given over the lower lumbar vertebrae and sacrum, with no relief of pain. Two days before readmission, after several hours of malaise, the patient noticed pain in the right lower quadrant of the abdomen. There had been no nausea or vomiting.

Tenderness, voluntary spasm and rebound pain were elicited in the right lower quadrant. The white-cell count was 8800.

A laparotomy was done, and an acutely inflamed appendix was removed. Convalescence was uneventful.

*Fifth admission* (four months later) Several weeks after operation, the pain became much worse, with radiation in a band-like manner around the anterior abdominal wall. There was considerable spasm of the sacrospinalis musculature, with limitation of flexion, extension and lateral bending of

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program appears elsewhere in this issue of the *Journal*. That an unusual opportunity for postgraduate instruction will be provided is evidenced by those who have signified their willingness to serve as chairmen. All who take part in the program are generously donating their time.

Although this series of lectures is primarily intended for the general practitioners and returned medical officers of Greater Boston, any licensed physician may enroll, and is urged to do so, there is no registration fee. All who plan to attend should enroll either by mailing the return postcard that has already been sent to all physicians in Massachusetts or by communicating directly with the Committee on Postgraduate Medical Education, Massachusetts Medical Society, 8 Fenway, Boston 15.

## CLINICAL INVESTIGATION BY THE VETERANS ADMINISTRATION

A PAPER published elsewhere in this issue of the *Journal* is a token of the vast amount of useful medical information in the records of the Veterans Administration that is ripe for harvesting if pains are taken in the cultivation of the field. The problems are numerous, and the numbers of disabled veterans are large in almost every category. Furthermore, there are already able and far-sighted physicians in the Veterans Administration who are anxious to utilize to the full the golden opportunity that now presents itself in the adequate follow-up study of the cases under their jurisdiction, both for the sake of the patients themselves and for the sake of new knowledge, which is certain to come if the study is well carried out.

In the cardiovascular field alone one can list five major problems that are in urgent need of concentrated follow-up study, which should be possible from the wealth of material under the care of the Veterans Administration: rheumatic fever and its effect on the heart, hypertension, early coronary heart disease, peripheral vascular diseases and neurocirculatory asthenia. Much could be learned from a detailed study of the patient under the age of forty years who is afflicted with angina pectoris or acute coronary occlusion, and this type of case

## REFRESHER COURSE FOR PHYSICIANS

THE attention of all physicians in Massachusetts is called to the series of review lectures that has been arranged for the Greater Boston area by the Subcommittee on Postgraduate Medical Education of the Postwar Planning Committee of the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health. In contrast to the method employed in the outlying districts, whereby a team of instructors gives an intensive course of talks at several localities in the district three or four times a year, this series will comprise four lectures of approximately forty-five minutes each on Mondays and Wednesdays, beginning February 18 and ending May 15. The tentative



**DR AUFRANC** We have a forty-one-year-old man who, over two years' observation, had more or less constant pain in the back. During that time x-ray studies gradually pointed out a lesion in the lumbar spine, which at the last examination consisted chiefly of destruction, with some production of bone in one film. The anterior portion of the body of the vertebra showed sequestration, so that the differential diagnosis seems to narrow down to a few things, the likeliest one of which is infection. The slow development of the destruction may well point to some malignant tumor, metastatic or primary, but the fact that he had had episodes of chills and fever seems to suggest an infectious process rather than a tumor. The radiation of pain around the thighs and to the anterior abdomen may well have been accounted for by slightly increasing abscess formation anteriorly around the bodies of the vertebrae involved.

One of the most frequent types of infection at this age is tuberculosis, and the fact that this man had sequestral formation fits in with that possibility. Other types of low-grade infection, such as staphylococcal infection, typhoid fever and brucellosis, should also be considered. The gradual spread of hypesthesia and numbness is further evidence pointing to a small slowly growing abscess somewhere. I believe that the dull pain on the right side may be attributed to the operation for kidney stone. Among the other less likely infections that one might think of is echinococcal cyst, a case of which I had not seen until I was in the Army, but now that I am out, I suppose that I should forget about it.

Among the types of tumor to be considered are primary carcinoma, metastatic cancer and possibly hemangioma. If it were hemangioma, it should have shown up earlier. There was no apparent source for metastatic disease: the gastrointestinal system was negative, and the prostate and the thyroid gland, which was explored once, were negative. So more than likely we can rule out tumor.

There is one other possibility, but it may have no bearing on the case, namely, that a small sponge was left in the wound at the time of the kidney operation and that it eventually resulted in a small abscess in the body of the vertebra, indicated by destruction around the body of the vertebra. I am not sure, however, that such an abscess would produce that much bone destruction.

My diagnosis is an infection — most probably not tuberculosis because of the slow rate of onset and the absence of tubercle bacilli, although I do not know that the latter rules it out. It was possibly osteomyelitis of the spine, with sequestral formation and a small abscess. There is no note concerning what was found at the time of appendectomy or whether the area was palpated, so there might have been a mass that was missed. The second possibility is tuberculosis.

**DR MARIAN W ROPES** This patient was a problem to us for two years. During the first part of the observation we hunted hard for a malignant tumor, since we thought that this was the likeliest explanation, but we failed to obtain any evidence other than the elevated phosphatase, which had persisted since the parathyroidectomy. The other two possibilities considered were rheumatoid spondylitis and tuberculous infection of the spine. Incidentally, the record does not describe the improvement that took place last winter, at which time he became almost symptom free and was able to work. At the time of this improvement I thought that rheumatoid spondylitis was probably the best explanation, but with the subsequent developments I thought that malignant disease or tuberculous infection were the two likeliest possibilities. The x-ray appearance never seemed quite satisfactory for either of these. The gradual development over the course of two years was surely surprising, particularly when there was no demonstrable x-ray change until the last few months.

**DR CHARLES L SHORT** I know the diagnosis, but I might say that, on seeing the patient after one of the operations, I thought that perhaps the pleurisy that he had had might have been considered in the differential diagnosis, in that way, perhaps on the basis of probability, the correct diagnosis might have been made.

**DR RICHARDSON** To me this case represents the value of a healthy amount of ignorance. I did not know enough to be puzzled very much. I said that this patient had a lesion of the bone, that he had had it for a long time and that he had also had recurring pleurisy with effusion, all of which to me meant tuberculosis. I advised against an operative procedure because I thought that if it were tuberculosis he might develop a sinus tract and difficulty in healing, I therefore suggested therapeutic doses of radiation. I did not realize that he had already been treated by x-ray.

#### CLINICAL DIAGNOSES

Rheumatoid arthritis  
Metastatic malignant disease?  
Tuberculous infection of spine?

#### DR AUFRANC'S DIAGNOSIS

Osteomyelitis of spine?  
Tuberculosis of spine?

#### ANATOMICAL DIAGNOSIS

Tuberculosis of spine

#### PATHOLOGICAL DISCUSSION

**DR BENJAMIN CASTLEMAN** At operation the surgeon encountered caseous tuberculosis, which was obvious even on gross examination. The slides confirmed that diagnosis. The fact that we were unable to recover tubercle bacilli from the pleural effusion does not rule out tuberculosis.

chemical mediation of nerve impulses, and in his last years to investigations "on the phenomena of a pace-maker in the rhythmic pulsations of the cerebral cortex"

Only World War I interrupted the continuity of his researches. The years 1917 and 1918 were spent in France and England, with a final rank of lieutenant colonel, and resulted in his brilliant studies on traumatic shock. These years were followed by an intense interest in world science and the freedom necessary for the cultivation of scientific pursuits. Since then he maintained that "a close relation exists between democracy and science" and "between liberty and democracy"

He acted on his convictions. He was the national chairman of the Medical Bureau to Aid Spanish Democracy, a member of the Joint Anti-Fascist Refugee Committee and the president of the American-Soviet Medical Society. Six months as visiting professor at Peking Union Medical College in 1935 led him later to become president of the American Bureau for Medical Aid to China and a director of the United China Relief organizations. He was foreign secretary of the National Academy of Sciences.

While a guest of the Russian Government, following his year in China, he had the courage to state his convictions regarding conditions essential for scientific progress in an address before the International Physiological Congress held in Moscow.

Another expressed conviction of Dr Cannon's was that "it is important for science to be understood in a democracy." Hence, among his books were four published for lay readers — three based on the results of his own and his collaborator's researches and one, his last, fortunately largely biographical, a description of the life of a scientist.

The broad application of Dr Cannon's investigations is indicated by his induction into membership in diverse special medical societies — the American Gastroenterological Association, the American Psychological Association, the American Psychopathological Association, the Association for the Study of Internal Secretions and the Société de Psychologie (Paris).

His travels, foreign lectureships, exchange professorships and attendance at medical meetings in all lands made Cannon the man as well as Cannon the scientist a truly international figure. In visits abroad, contacts that to most persons would have meant pleasant but temporary relations with Cannon resulted in permanent friendships. He had warm lifelong friends among distinguished scientists of many countries — Britain, France, Germany, Russia, Spain, Italy, the Argentine, Mexico and China. He had the broad sagacity of Benjamin Franklin and the democracy of Abraham Lincoln. His geniality, quick wit and delightful sense of humor enlivened any group he chanced to join and made him the best of companions on all occasions.

Every possible kind of scientific honor came to Dr Cannon — from this country, the Distinguished Service Medal, from England, Companion of the Bath, and from all civilized countries, memberships in learned societies and honorary degrees.

In the fall of 1931, Dr Cannon completed twenty-five years of service as George Higginson Professor of Physiology. The occasion was celebrated by the presentation of his portrait to the University and by afternoon and evening exercises at which the country's most distinguished physiologists and President Lowell spoke.

His achievements and honors did not change him. He remained always the approachable, honest, simple, devoted, modest gentleman, worthy of the pride of his university and his nation.

*Who's Who* contains a lengthy list of Dr Cannon's degrees, honors, decorations, honorary lectureships and societies, ten of his honorary degrees, however, are not mentioned, five of them from foreign universities. Also omitted are honorary memberships in fourteen foreign scientific societies and academies.

Dr Cannon realized more and greater satisfactions from life than come to most — in achievement, in the admiration and affection of his fellow-men and in his family. In spite of his many diversified activities related to his scientific and humanitarian activities, Dr Cannon was a devoted family man. He also found time to give to old friends and for the cultivation of new friendships. Regretful notices of Dr Cannon's death have come to the University from many lands.

S B W

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

CAVANAUGH — Mortimer T. Cavanaugh, M.D., of Great Barrington, died October 7. He was in his seventy-fourth year.

Dr Cavanaugh received his degree from Baltimore Medical College in 1898. He was a fellow of the American Medical Association.

His widow survives.

GOODWIN — James J. Goodwin, M.D., of Clinton, died December 29. He was in his eighty-first year.

Dr Goodwin received his degree from the Jefferson Medical College of Philadelphia in 1892. He retired in 1943. He was a member of the American College of Surgeons and the New England Surgical Society.

His widow and three sons survive.

KAPLAN — Boris Kaplan, M.D., of New Bedford, died December 25. He was in his fifty-seventh year.

Dr Kaplan received his degree from Saratov Medical Institute, Russia, in 1918. He was a member of the National Gastroenterological Association and a fellow of the American Medical Association.

His widow and two children survive.

is already represented by hundreds of persons on the rolls of the Veterans Administration

Whatever is learned from such follow-up studies of the disabled veterans will be of immediate practical use in the diagnosis and treatment of the veterans themselves. It is not at all a matter of idle academic curiosity and experimentation. Hence, anything that can be done to foster the proper development of the medical work of the Veterans Administration will improve the care of the men and women who have helped so much in saving the world from tyranny, and will simultaneously advance medical knowledge. It is hoped that such a rare opportunity will not be allowed to slip, as it did after World War I.

## OBITUARY

### WALTER BRADFORD CANNON

1871-1945

Many generations of Dr. Cannon's forebears — on both sides — lived in America. Both lines were characterized by initiative and courage, and men and women among them were pioneers in the westward extension of American frontiers. Dr. Cannon was thoroughly and gloriously American.

In personality he was direct, absolutely genuine without tinge of artificiality, formal only when necessary to meet the amenities of special occasions. He met persons in all walks of life from the lowliest of employees to the world's most distinguished in science and administration, confidently, simply and directly, making real and sympathetic contact by virtue of his diversified experiences, his comprehensive intelligence and his love for all human beings. Competent in highest degree to appraise character and achievement, praise often came from him, condemnation rarely — and never expressed at large. One of the world's great scientists, he was for many years one of the most beloved and revered professors at the Harvard Medical School.

Dr. Cannon was born in Prairie du Chien, Wisconsin, on October 19, 1871. Much of his boyhood was spent in Wisconsin and Minnesota in essentially rural surroundings, whence came his resourcefulness in mechanics and interpretation of natural phenomena. Simple out-of-door pursuits — canoeing, walking and mountain climbing — and working with tools remained always his chief recreational activities. The whole of Dr. Cannon's adult life was spent as a student and faculty member at Harvard. In high school at St. Paul, Minnesota, and in Harvard College he was distinguished for high scholarship and extracurricular activities. In 1906, six years after graduation from Harvard Medical

School he was made George Higginson Professor of Physiology — a record in rapidity of appraisal by the medical school. Unusual too for that day was a young professor who had not been directly exposed to European influences. His early recognition by the University was understandable for he was already engaged in independently conceived research, the pursuit of which occupied him for the remaining forty years of his life and which, step by step, led him to become the world's outstanding investigator in the highest plane of physiologic research, that of the integration of many body systems in relation to the emotions.

His retirement in 1942 brought no interruption in research, only a move into the Biological Laboratories in Cambridge. For several months preceding his death, Dr. Cannon worked in Mexico City in order to collaborate with a favorite pupil, applying to research in neurophysiology of the brain information obtained from their researches on the peripheral systemic and sympathetic nervous systems.

A truly great school of physiology developed at Harvard because of Dr. Cannon's eminence as a scientist and because of those personal qualities that inspire respect and affection through inspirational guidance of pupils. More than forty persons holding professorial or equivalent rank in important universities and institutions have been definitely exposed to Dr. Cannon's personal influence in their work. As a teacher of medical undergraduates he was a powerful influence and drew many talented men into his laboratories. He became the outstanding personality in physiology in this country and was one of the greatest figures in the Harvard Medical School in the period of its greatest progress.

Years ago, after carefully weighing his opportunities for service to the medical school, he declined the deanship. Always, however, his influence and services in the councils of the medical school were great. His judgment was always detached, his decisions prompt and productive of action. He was ever ready to fight in support of his convictions.

Dr. Cannon's first bit of research was done with Professor C. B. Davenport, while an undergraduate in college. In 1898, while a second-year medical student, he began his studies of the movements of the gastrointestinal tract by means of radio-opaque substances and x-rays. He soon discovered the great effect of the emotions on the gastrointestinal movements. Continued reflective thinking on the results of each set of experiments led to his studies on the sympathetic nervous system by itself and in co-operation with the glands of internal secretion. Most of the present-day knowledge regarding the physiologic significance of the sympathetic nervous system and its integration with the activities of ductless glands is the result of research completed by him and his collaborators before his sixtieth year. Subsequent, and to him obvious, lines of research led to his great contributions on the

The success of this treatment entirely depends on the efforts of the person using it. If the exercises are not performed regularly and often for a period of months, it is of little value. It takes time to build up the tone and strength of the facial muscles, as it does with any other group of muscles in the body.

I am submitting this idea not as a claim for the cure of cne but as a useful adjunct in its treatment.

NEIL C STEVENS

Walpole, New Hampshire

## DERMATITIS FROM DDT SOLUTION

To the Editor: The public has waited impatiently for the much publicized DDT—dichloro-diphenyl-trichlorethane. Its use is, however, attended with a certain amount of risk, not so much because of the DDT itself but because of the solvents used in its preparation. The latter include crude kerosene, refined odorless kerosene, soy-bean oil, cyclohexylamine, xylene, acetone and ether. The most popular one is deodorized kerosene. This has not only the hazard of inflammability but also produces a dermatitis if it remains in contact with the skin for a sufficient length of time and under certain conditions, as shown by the following case report.

A fifty-two-year-old janitor presented a rash on the face, neck and back of hands of two weeks' duration. He showed erythema, fine vesicles and papules, the so-called "helmet type" of eruption frequently seen after exposure to irritating dust or fumes. History revealed that for several days shortly before the onset he had used as a spray a new preparation for killing insects. After each spraying episode his skin itched, until finally his face broke out in a rash. In the course of his occupation he also used floor wax. Investigation revealed that the spraying solution consisted of 5 per cent DDT, thiante and the bulk highly refined kerosene. He was given treatment and later patch tested with the following substances: the DDT solution, floor wax, pure powdered DDT, and a control. The last was prepared by applying the DDT solution to a cloth and allowing the solvent to evaporate before the cloth was applied to the skin. There was no reaction from the floor wax, pure powdered DDT or control, but there was a marked erythema and vesiculation at the site of the DDT solution, the erythema extending around the dressing for an area of over 2 cm. on either side.

Although DDT apparently does not cause a dermatitis, the solvents may and in spraying these solutions persons should exercise great care and protect the exposed areas of the skin.

JOHN G. DOWNING, M.D.

520 Commonwealth Avenue  
Boston 15

## NEW REGULATIONS OF DEPARTMENT OF MENTAL HEALTH

To the Editor: Under authority of Section 10 of Chapter 123 of the General Laws, the Department of Mental Health hereby establishes the entire state of Massachusetts, excepting the City of Boston, as the state-hospital district for children fifteen years of age or younger.

Commitments to Walter E. Fernald State School, Wrentham State School, Belchertown State School and Monson State Hospital will remain as before.

Effective January 1, 1946, no children fifteen years of age or younger are to be admitted to any of the following state hospitals: Boston, Danvers, Foxborough, Gardner, Grafton, Medfield, Northampton, Taunton, Westborough and Worcester.

Children fifteen years of age or younger from the City of Boston may be admitted to the Boston Psychopathic Hospital for short periods of study. Facilities for prolonged care of these children will be available only at the Metropolitan State Hospital, and if the need for prolonged care is anticipated, such children should be sent directly to the Metropolitan State Hospital. Boston committing courts may commit such children directly to the Metropolitan State Hospital without a waiver.

The intent of the new plan is to permit proper segregation of children from mentally ill adults and to provide adequate educational and recreational facilities for these children.

CLIFTON T. PERKINS, M.D., Commissioner  
Department of Mental Health

100 Nashua Street  
Boston

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Peripheral Nerve Injuries: Principles of diagnosis.* By Webb Haymaker, Capt., M.C., A.U.S., neuropathologist, Army Institute of Pathology, Washington, D.C., and Barnes Woodhall, Maj., M.C., A.U.S., chief, Neurosurgical Section, Walter Reed General Hospital, Washington, D.C. 8°, cloth, 227 pp., with 225 illustrations. Philadelphia: W.B. Saunders Company, 1945. \$4.50.

The authors have incorporated in this work the newest information concerning their subject based on army experience. The book is intended for medical officers, as well as for medical students and civilian physicians who will be required to treat patients afflicted with nerve injuries. The volume is divided into three sections: the first discusses the principles of innervation, the second, the examination of the patient, and the third, the clinical features of plexus and peripheral nerve injuries. The text is copiously illustrated with photographs and line drawings. The book is printed on good paper, with a good type, and is easy to read. It is recommended as a reference text for all medical libraries.

*Textbook of Abnormal Psychology.* By Roy M. Dorcus, associate professor of psychology, University of California at Los Angeles, and G. Wilson Shaffer, dean of the College of Arts and Sciences, lecturer in psychology and professor of health and physical education, Johns Hopkins University, and psychologist Sheppard-Enoch Pratt Hospital, Towson, Maryland. Third edition. 8°, cloth, 547 pp., with 5 plates. Baltimore: Williams and Wilkins Company, 1945. \$4.00.

The publication record of this volume speaks well for its authority as a text on its subject. First printed in 1934, the second edition was published in 1939, and the third edition of 1945 is the eleventh printing of editions and reprints. The authors believe that there has not been any marked change in directional lines during the past five years and therefore have incorporated new material in the existing framework that has stood the test of time. Some of the material has been rearranged to obtain greater clarity for the student. The text has been written for advanced students in psychology, premedical students and medical students who already have had instruction in psychology. Scientific rather than popular terminology has been used wherever possible. An extensive bibliography of 833 references has been appended to the text, 365 of these have been added from the literature of the past five years. The text is well documented, and the book should serve as a reference source for all medical and university libraries.

*Radiologic Examination of the Small Intestine.* By Ross Golden, M.D., professor of radiology, College of Physicians and Surgeons, Columbia University, and director of the Radiological Service, Presbyterian Hospital, New York City. 4°, cloth, 239 pp., with 75 illustrations. Philadelphia: J.B. Lippincott Company, 1945. \$6.00.

The material contained in this volume has been assembled over a period of many years, and the text is based on instructional courses given by the author at various radiologic society meetings. The book has been written from the viewpoint of diagnosis, and no attempt has been made to discuss the treatment of disease. A comprehensive bibliography and an adequate index have been added to the text. The volume is well printed, with a good type, on good paper, making it easy to read comfortably.

*Mass Radiography of the Chest.* By Herman E. Hilleboe, M.D., medical director and chief, Tuberculosis Control Division, United States Public Health Service, and professional lecturer on tuberculosis control, George Washington University School of Medicine, Washington, D.C., and Russell H. Morgan, M.D., medical officer-in-charge, Radiology Section, Tuberculosis Control Division, United States Public Health Service, and assistant professor of roentgenology (on leave

**LEONARD** — Edward D. Leonard, M.D., of Newton Centre, died December 15. He was in his sixty-first year.

Dr. Leonard received his degree from Harvard Medical School in 1913. He joined the Newton Hospital staff in 1916 and became surgeon-in-chief in 1933, holding that position until last year, when he became an emeritus member of the staff. He was a fellow of the American Medical Association and a member of the American College of Surgeons.

His widow, a son and two sisters survive.

**McNAMARA** — John J. McNamara, M.D., of Brockton, died January 3. He was in his seventy-fifth year.

Dr. McNamara received his degree from Tufts College Medical School in 1900. He was formerly president of the Plymouth District Medical Society. He was a member of the Massachusetts Examining Physicians Association and a fellow of the American Medical Association.

Two brothers and a sister survive.

## NEW HAMPSHIRE MEDICAL SOCIETY

### DEATHS

**ABBOTT** — Clifton S. Abbott, M.D., of Laconia, died December 10. He was in his seventy-fourth year.

Dr. Abbott received his degree from Dartmouth Medical School in 1894. He had served as president of the New Hampshire Medical Society. He was a member of the American College of Surgeons and a fellow of the American Medical Association.

A sister survives.

**CUTLER** — Charles H. Cutler, M.D., of Peterborough, died December 22. He was in his seventy-ninth year.

Dr. Cutler received his degree from the University of Vermont College of Medicine in 1892. He was a fellow of the American Medical Association.

His daughter and two sisters survive.

**TAYLOR** — Herbert L. Taylor, M.D., of Portsmouth, died October 24. He was in his sixty-ninth year.

Dr. Taylor received his degree from Jefferson Medical College of Philadelphia in 1902. He was a fellow of the American Medical Association and the American College of Surgeons.

His widow and a daughter survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### DISTRIBUTION OF PENICILLIN STOPPED

Effective February 1, the distribution of sodium penicillin by the Massachusetts Department of Public Health to private physicians for the treatment of gonorrhea will be temporarily discontinued, owing to the present shortage of this product.

When sufficient quantities have been accumulated to assure a surplus over the quantity needed by state institutions and co-operating clinics, distribution to private practitioners will be resumed.

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Worcester	January 18	John W. O'Meara
Pittsfield	January 21	Frank A. Slowick
Fall River	January 28	David S. Grice
Hyannis	January 29*	Paul L. Norton

\*Day changed

Physicians referring new patients to the clinics should get in touch with the district health officer to make appointments.

## MISCELLANY

### REFRESHER COURSES AT HARVARD FOR DISCHARGED MEDICAL OFFICERS

Harvard Medical School will offer a series of six month refresher courses for medical officers discharged from the armed forces. These courses, under the supervision of Dr. Eugene C. Eppinger, assistant dean in charge of Courses for Graduates, will emphasize current scientific knowledge and theories and advances in the medical field. Instruction will be given by the regular members of the preclinical and clinical departments of the medical school. The first course is scheduled to begin on February 1.

In offering these courses, the medical school is attempting to assist physicians who, on separation from the services, wish to obtain the latest knowledge in the broad field of medicine in preparation for re-entering a civilian medical career.

## CORRESPONDENCE

### FACIAL EXERCISES AS AN AID IN THE TREATMENT OF ACNE

*To the Editor*—An important factor in the causation of acne is the accumulation of material in the sebaceous glands; the excretion does not keep pace with its formation. A black head forms, which sooner or later becomes infected, and a simple result.

Acne usually occurs on the face and neck and between the shoulder blades. Sometimes it appears on the chest. It generally does not occur on the arms, abdomen, lower back, buttocks or legs. In other words the lesions are found on the parts of the body that get little exercise. The face, where it occurs most frequently, is hardly exercised at all.

It is reasonable to suppose that, if the tone of the muscles were increased and strengthened, the excretion of sebaceous material would be facilitated. Its excretion would keep pace with its formation, and there would be no chance for a black head to form. Also the circulation would improve, which is an additional factor in the prevention of infection.

The required exercises to improve muscular tone are simple and easy to perform. First, the lower jaw is drawn down as far as possible and the face is stretched. This is done twenty or thirty times and repeated at convenient times during the day. This also exercises, to some extent, the muscles of the neck. The second exercise is the raising and lowering of the skin of the forehead. Thirdly, the lower jaw is pushed forward and backward many times. This exercises not only the muscles of the lower jaw but also those of the neck. And, finally, the neck muscles are exercised by bending the head forward and backward and by turning it from side to side.

Obviously, this treatment is entirely harmless and can be used in conjunction with other methods. It not only appears to be an aid in the cure of acne but also better the patient's looks, by improving the texture and color of the skin and by increasing the tone and strength of the facial muscles.

Acne is rare in this part of the country, and I have been able to experiment on only five cases. The first was that of a high-school boy of sixteen who had the worst case of acne that I have ever seen. The cheeks, forehead, chin and neck were covered with large and small pustules. The skin was greasy and rough and pasty. Treatment was begun three and a half months ago. The patient was much ashamed of the condition of his skin, he has been most co-operative and has faithfully performed the exercises. No other type of treatment was given during this period. After about three weeks the condition of his skin began to improve, and this has continued steadily since then. I saw him two weeks ago. His face was entirely free of pimples. The skin was still rough and scarred, but it had lost its pasty, greasy appearance and was firm and tight. The expression of his face had changed, and his looks were considerably improved. Acne was still present on the neck, but to a lesser degree than when I first saw him, possibly because he had not been able to exercise the muscles of his neck so efficiently as his facial muscles.

The other four cases treated by this method had moderate to mild degrees of acne. No other treatment except the exercises was employed. Although they have been using the treatment from only one to three months, all have shown definite improvement.

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## HODGKIN'S DISEASE\*

### VII. Treatment and Prognosis

HENRY JACKSON, JR., M.D.,† AND FREDERIC PARKER, JR., M.D.‡

BOSTON

**T**HIS concluding paper of the series on various aspects of Hodgkin's disease concerns treatment and prognosis

#### TREATMENT

##### *Hodgkin's Paragranuloma*

It is difficult to give advice on the treatment of Hodgkin's paragranuloma. In view of the apparently localized nature of the disease in many cases and the excellent results of surgery in 2 of our cases, it seems reasonable to advocate radical dissection, followed by irradiation whenever the condition seems to be sharply confined to a readily accessible region. It must be pointed out, nevertheless, that there have been recurrences in 3 of 5 cases in which surgical excision was practiced, and this fact indicates that excision should be followed by prophylactic irradiation. Of the 2 patients who have been subjected to this routine, one is alive and entirely free from signs or symptoms thirty-four years after the onset of her disease, and the other, having remained symptom-free for twenty-four years, developed Hodgkin's granuloma and died three years later. If radical dissection does not appear to be warranted, fairly heavy doses of x-ray are indicated provided that not more than one area is involved.

##### *Hodgkin's Granuloma*

There is no specific treatment for Hodgkin's granuloma, nor is there likely to be one until its cause has been found. There are, however, a number of therapeutic measures that may be expected to prolong life and that will certainly alleviate the symptoms, often for a long period of time.

Three points should be borne in mind. First, in the great majority of cases, by the time the patient is first seen the disease has affected more than one organ. Second, virtually every organ and tissue may be involved sooner or later, and the utmost diligence must be exercised by the clinician to discover as early as possible any involvement of internal organs, so that appropriate therapeutic measures may be promptly instituted. Third, the disease may begin insidiously in an isolated and localized focus, and it is in all probability a circumscribed process at onset. This at least is our opinion, although we recognize that it is not shared by many students of the subject. In short, we believe that Hodgkin's granuloma has its origin in a single isolated focus, often, unfortunately, internal, and spreads insidiously, although rather rapidly, eventually involving many organs.

It is thus clear that if one is to have any hope of actually curing the condition, it must be discovered in its earliest stages and be promptly treated with the utmost energy. It is equally clear that both the clinician and the radiologist must constantly be on the lookout for evidence of involvement of internal organs, and must not content themselves with the gratifying results of treatment directed solely to superficial lymph nodes, which are in most cases merely the visible expression of an internal lesion. This point has become increasingly obvious in recent years.

A biopsy should be performed prior to therapy in all cases in which it is feasible. Unless this is done, and unless the removed lymph node is properly fixed and stained, one cannot be certain of the diagnosis, nor can the ultimate results of any form of therapy be accurately judged. Furthermore, a careful and complete physical examination, together with routine blood studies and x-ray examination of the chest, should be done in all cases at the first visit. Additional x-ray or laboratory studies may be indicated in specific cases.

\*From the Thorndike Memorial Laboratory, the Second and Fourth Medical Services (Harvard) and the Mallory Institute of Pathology, Boston City Hospital; the Department of Medicine, Harvard University, and the Pondville Hospital, Massachusetts Department of Public Health. This is the seventh and concluding article of a series of seven papers covering the various aspects of Hodgkin's disease.

†Assistant professor of medicine, Harvard Medical School; associate physician, Thorndike Memorial Laboratory, Boston City Hospital; physician, Pondville Hospital, Wrentham, Massachusetts.

‡Associate professor of pathology, Harvard Medical School; pathologist-in-chief, Boston City Hospital.

of absence), University of Chicago 12°, cloth, 288 pp., with 93 illustrations Chicago The Year Book Publishers, Incorporated, 1945 \$3.50

The purpose of this small book is to bring together literature on mass radiography of the chest in one volume and to provide a general handbook of methods

*The History of Surgical Anesthesia* By Thomas E. Keys, M.A. With an introductory essay by Chauncey D. Leake, M.D., and a concluding chapter, "The Future of Anesthesia," by Noel A. Gillespie, M.D. 8°, cloth, 191 pp., with 43 illustrations. New York Schuman's, 1945 \$6.00

Major Keys has written a short history of the development of anesthesia from its earliest beginnings to the present time. Dr. Chauncey D. Leake has provided an interesting introductory essay in which will be found much material supplementing the text of Keys, and including his personal notes on anesthesia. In commenting on anesthesia collections, Dr. Leake omitted mentioning the valuable collection of the Boston Medical Library. The appendices contain a bibliography of selected references, a chronology of events relating to anesthesiology and allied subjects dating from 4004 B.C. to 1944 A.D., with a list of sources for this chronology, and a list of selected references for a history of surgical anesthesia arranged by subject and also arranged by author. In an appendix Dr. John F. Fulton discusses the Morton and Warren tracts on ether (Letheon). A comprehensive index is provided, and the text is well printed, with a good type, on good paper in the characteristic Schuman style.

*The Modern Medical World. Portraits and biographical sketches of distinguished men in medicine* By Solomon R. Kagan, M.D. 8°, cloth, 223 pp., illustrated. Boston Medico-Historical Press, 1945 \$6.00

This volume is a continuation of a series of other volumes on medical biography written by Dr. Kagan. Although there is an index of names, an alphabetical arrangement of the text would have been more useful than the present haphazard set-up. The selection of names contains many not commonly found in medical literature. This volume should be useful in all historical collections.

*Yellow Magic. The story of penicillin* By J. D. Ratcliff. 12°, cloth, 173 pp. New York Random House, 1945 \$2.00

In this popular book Mr. Ratcliff tells the story of how penicillin was discovered and developed from the laboratory stage through the stage of clinical testing and trials to the present-day commercial production. The early chapters of the book are devoted to a history of the subject. There follow special chapters on the use of penicillin in the treatment of syphilis and gonorrhea, and in war wounds. One chapter is devoted to the work of the "heartless man in Boston," Dr. Chester S. Keefer. Dr. Keefer has written a foreword, and Dr. Morris Fishbein an introduction to the text. Mr. Ratcliff is a competent authority in the field of science, and he carefully prepared himself by visiting laboratories, hospitals and manufacturing plants preparatory to writing his short manual. The manual should prove useful to all medical and public libraries as a quick reference source on the history of penicillin.

*The Newborn Infant. A manual of obstetrical pediatrics* By Emerson L. Stone, M.D., associate clinical professor of obstetrics and gynecology, School of Medicine, Yale University, and attending obstetrician and gynecologist to the New Haven Hospital. Third edition, 12°, cloth, 314 pp., thoroughly revised. Philadelphia Lea and Febiger, 1945 \$3.25

This small book, first published in 1929, was originally the outgrowth of a short selective course of lectures given to the senior class of Johns Hopkins University School of Medicine. The work has two principal objectives to correlate and arrange in an orderly fashion a mass of data that are otherwise scattered through the medical literature and to emphasize the obstetrician's viewpoint and responsibility. The present revision aims to review concisely the accepted principles of physiology and pathology in the newborn infant and

to incorporate the added knowledge of the past decade in the field of medical practice. The text is well written, has a good index and should prove useful as a resume of its subject.

*The Falling Sickness. A history of epilepsy from the Greeks to the beginnings of modern neurology* By Owsei Temkin, M.D., associate professor of the history of medicine, Johns Hopkins University. 4°, cloth, 380 pp., with 7 illustrations. Baltimore Johns Hopkins Press, 1945 \$4.00

Dr. Temkin, in this scholarly monograph, has written a history of epilepsy from the time of earliest antiquity to the time of Hughlings Jackson, about 1880. An extensive bibliography arranged alphabetically is appended to the text. The book is well printed, with a good type, on good paper and written in an interesting manner. It should be in all medical libraries and should prove interesting for public collections.

## NOTICES

### ANNOUNCEMENTS

Dr. Hollis L. Albright has resumed practice at 412 Beacon Street, Boston.

Dr. John J. Cincotti, recently discharged from military service, announces the opening of an office at 475 Commonwealth Avenue, Boston, for the practice of general surgery.

Dr. Robert J. Joplin, having recently returned from overseas duty with the Navy, announces the reopening of his office at 372 Marlborough Street, Boston, for the practice of orthopedic surgery.

Dr. Jost J. Michelsen announces the opening of an office at 311 Beacon Street, Boston, for the practice of neurological surgery.

Dr. Robert S. Palmer announces his return to the practice of internal medicine at 330 Dartmouth Street, Boston.

Dr. Theodore C. Pratt is resuming the practice of general surgery at 1101 Beacon Street, Brookline.

Dr. Salvatore Scelso announces the reopening of his office at 395 Commonwealth Avenue, Boston.

Dr. Grantley W. Taylor announces his release from military service and his return to private practice at 264 Beacon Street, Boston.

Dr. Winthrop Wetherbee, Jr., recently discharged from the Army, is resuming the practice of general medicine at 24 School Street, Boston.

### SYMPOSIUM ON COMMUNICABLE-DISEASE CONTROL

The North Metropolitan District of the Massachusetts Department of Public Health, in co-operation with Boston University School of Medicine, will conduct a meeting "Looking Ahead in Communicable-Disease Control" on January 22 at Boston University School of Medicine, 80 East Concord Street, Boston. The morning session will be held from 10:00 a.m. to 12:00 noon, and the afternoon session from 2:00 to 4:30 p.m. The purpose of the meeting is to present to health workers and all others interested the recent advances in communicable-disease control. Discussions on biological, treatment with sulfa drugs and antibiotics, isolation and quarantine have been planned. In addition, a demonstration of nursing technique in the home and hospital will be presented, with a discussion by a bacteriologist and an epidemiologist.

(Notices continued on page xix)

the patient may seem at the time to be at death's door. Many patients have rapidly and markedly failed, only to return to comparative health when hospitalized, transfused and given appropriate irradiation. Gilbert<sup>1</sup> cites such a case from his own practice.

To obtain the best co-operation and thus the best results, it is wise to give the patient a general idea of what may be expected of x-ray therapy. It is not necessary to name the disease, it would obviously be unwise to picture the final outcome, and it is unnecessary to dwell on details. It is, however, proper to point out that the outward manifestations of the disease will diminish or even disappear, but with a warning that the same disease process may subsequently reappear in another place and that any untoward sign or symptom should be immediately reported. Only thus and by repeated routine examination can one hope to keep the disease in abeyance.

The question of marriage and pregnancy is, of course, of great importance. Both should probably be advised against, but, as Gilbert says, "these events occur in spite of us." If pregnancy should take place, it is necessary to decide whether it should be terminated. This question cannot be categorically answered. Three of our patients have become pregnant. One, a multipara, was aborted at her own request. She was alive and free from symptoms three years later. The other two, both primiparas, gave birth to normal babies, and each was well one and two years later, respectively, both children remaining well. Gilbert has had a similar although more extensive experience. The ultimate fate of the offspring cannot, of course, be foretold, but the present data seem to justify allowing pregnancy to go to term provided that one or both of the parents realize the potentialities.

In assigning to the fundamental disorder signs and symptoms that may properly be attributed to it, enthusiasm must be tempered with a modicum of knowledge of general medicine. One of our patients, a sixty-year-old Armenian, with "small Latin and less Greek" said that he was unable "to pass the water." What more tempting, in view of the fact that his disease was widely disseminated, than to see as a cause of this complaint a granulomatous process in the prostate and to irradiate that organ. Forthwith, he was indeed, "unable to pass the water." It was with much relief and some chagrin that we witnessed a complete and lasting disappearance of his symptoms following a prostatectomy for the simple, benign prostatic hypertrophy of old age.

In almost all early publications concerning irradiation, it was stated that although the symptoms could thus be alleviated, life could not be prolonged. It has recently become increasingly apparent that this is not the case. We agree with Gilbert and

others that the average duration of survival is prolonged. In 1923, Desjardins and Ford<sup>4</sup> found that only a scant 10 per cent of their patients survived for more than five years. In 1932, Holfelder and Hummell (quoted by Gilbert<sup>1</sup>) reported that nearly 18 per cent of their patients had passed the five-year mark. In Gilbert's series, 34 per cent fell into this category.

The results of irradiation vary within wide and unpredictable limits, as a rule, they are fairly satisfactory. Generally speaking, however, bone lesions are less radiosensitive than are foci in other organs. Lesions of the sternum, however, usually show a satisfactory response. In any event, relief from pain is often striking, and in some cases bone regeneration and repair have been observed. That excellent results may be obtained in such cases is attested by the following case.

E. W., (P 1935), a 20-year-old man was admitted to the hospital on January 3, 1933. In September, 1931, he had noticed a "swollen gland" behind the left ear. One month later this became painful and other lymph nodes appeared in the left side of the neck. One of these was removed, and a diagnosis of Hodgkin's granuloma was made. During the next 5 years lymph nodes appeared from time to time in the neck, axillas and groins, but always diminished or disappeared after appropriate high-voltage x-ray treatment. In addition, the patient was periodically troubled by intense generalized itching, which was partially controlled by spray x-ray treatment and by viosterol in large doses. His general health however, continued to be good, and he remained mentally and physically active.

In June, 1936, the patient complained of pain, especially on motion, in the lower lumbar region. This was relieved by the administration of 60r by spray to the body anteriorly and 100 r posteriorly. In October of that year there were no palpable lymph nodes, and the patient's general condition was excellent, — although he had lost some weight, — but he complained of intense pain in the lumbar region, particularly on the right side.

Physical examination showed a marked lumbar scoliosis on the left side and intense contraction of the lumbar spinal muscles on the right side. X-ray films showed a destructive process of the bodies and transverse processes of the 1st and 2nd lumbar vertebrae. There was a slight degree of vertebral collapse. Six hundred roentgens was given over the involved area, and the pain completely disappeared. In January, 1937, there was some return of the pain but complete relief was again obtained after the administration of 400r to the lumbar region.

In May, 1937, the patient again complained of considerable discomfort in the lumbar region, and x-ray examination showed an increase of the destruction of the 1st and 2nd lumbar vertebrae. Nine hundred roentgens was given over the involved area, and in October there was evidence that new bone was being laid down in the bodies of the vertebrae and that fingerlike processes of new bone were reaching out into the soft tissue to bridge the existing defect. The radiologist noted that there appeared to have been an arrest of the process and a laying down of calcium deposits in the ligamentous structures surrounding the lateral portions of the 1st and 2nd lumbar vertebrae on the left.

The general result was that in spite of the bony destruction there was a partial and fairly effective ankylosis of the spine. Nine hundred roentgens more was given, and the patient continued to be in reasonably good health and was able to control the discomfort in the lumbar region by salicylates. In spite of the marked bone lesion he was able to swim, play tennis and ski, although he complained, with a smile, that a left hand telemark was hard to accomplish.

By October, 1939, the lesion of the lumbar spine had extended to include the body of the 12th dorsal vertebra. There was, however, no increase in symptoms, and the patient was still active in athletics 8 years after the initial symptoms.



The most valuable therapeutic measure is irradiation. On this point all are agreed, but there is no consensus concerning the best method of applying it. Indeed, it is clear that in a disease showing such diverse and protean manifestations and running such an unpredictable and variable course, this is almost inevitable. The treatment must necessarily be adapted to the individual patient, the results of therapy can be adjudged only over a long period of time and with due regard to the varied manifestations of the disease.

There are various schools of thought regarding the proper type of irradiation, and one may choose for oneself that which seems the most logical, the most promising and the most suitable.

Gilbert<sup>1</sup> has covered this entire subject with care, and to his article the reader is especially referred. A partisan of high-voltage x-ray, he advocates wide irradiation of the regions patently invaded as well as those suspected of invasion, and contends that it is essential to irradiate widely enough to be reasonably certain of subjecting the entire involved regions to the action of the rays. In consequence of his belief that local recurrences begin in granulomatous islands subjected to inadequate irradiation, his initial doses are relatively large. Panteleoroentgen therapy is, in his opinion, of more harm than good.

His therapeutic regime is briefly as follows. Diagnosis is made by biopsy whenever feasible. Involved areas and regions suspected of being involved by reason of the symptoms are irradiated, from 180 to 200 kilovolts being used through portals up to 20 by 20 cm. To each area are given fractional doses of approximately 200r every other day until the desired total has been delivered — a minimum total depth dose of 500r to each focus. The paravertebral, para-aortic and retroperitoneal nodes are irradiated if general signs, such as fever, pruritus and asthenia, persist after successful irradiation of apparently localized disease elsewhere. Treatment is renewed only if evidence of recurrence is seen.

Sixteen of Gilbert's 52 patients treated in this manner were still alive at the time of his report, of these, 9 (17 per cent of the total) had survived five years or more and 3 had survived for ten years or more.

In recent years, our own therapeutic approach has been similar to that of Gilbert. A 250-kilovolt machine is used. Each area involved or suspected of being involved is treated through a portal of sufficient size to embrace the entire field, in fractionated doses until the required amount has been given. It is probably best to give comparatively small doses to any given area if the disease is widespread, but many authorities believe that large, heavy doses should be given if the condition appears to be confined to one region. No further irradiation is resorted to unless there is a recurrence.

Recently, we have in certain selected cases used a supervoltage (1000-kilovolt) x-ray machine. It is too early to come to any conclusion concerning the relative merits of this method of irradiation. All patients are seen at frequent intervals, — two weeks to three months, — and great diligence is exercised in attempting to discover, by one means or another, any new focus of disease. Any persistent symptom or sign not explainable on other grounds is regarded as being due to Hodgkin's granuloma and appropriate irradiation is given. This is an important part of the treatment, irrespective of the exact type of irradiation used. Of the 35 patients in our series still alive on January 1, 1945, 17 (47 per cent) have survived for five years or more. Thus, 16 per cent of the patients in the entire series who were subjected to systematic treatment and adequately followed survived for five years or more.

It is our belief that the internist and the radiologist should care for the patient conjointly and that all details of x-ray therapy should be left to the radiologist. No matter what type of x-ray therapy is used, — and it is obvious that competent authorities advise varying methods of attack, — certain practical points should be borne in mind.

Extremely large mediastinal masses must be treated with great caution, for not infrequently they are extremely radiosensitive, in which event too rapid destruction by excessive amounts of x-ray may result in the organism's being flooded with products of necrosis, which may bring about highly toxic manifestations or even death.

The acute form of Hodgkin's granuloma, accompanied by high temperatures, an elevated white-cell count and the signs and symptoms of an acute infection, must be treated with great care and conservatism. A rapid rise in temperature calls for temporary cessation of therapy. The situation is somewhat analogous to that seen in acute leukemia.

The presence of active tuberculosis contraindicates irradiation of the lungs and mediastinum in the usual doses, as does renal insufficiency, especially if associated with nitrogen retention.

The presence of unexplained fever, vague gastrointestinal disturbances, fleeting abdominal pains, generalized itching or a persistently elevated white-cell count, with an increase of polymorphonuclear leukocytes, usually indicates the presence of diseased lymph nodes deep in the abdomen or in the para-aortic region, and irradiation of these areas often causes a remission of the symptoms.

We have been increasingly impressed with the wisdom of relentless treatment even in the face of what appear to be overwhelming odds. Of course a point is reached when further irradiation is fruitless and even harmful, but this does not usually occur until after many courses of treatment, and it is remarkable what may be accomplished in the relatively early stages of the disease even though

until the time comes when it can be truthfully said that operative interference is uncalled for. Too often one waits to see what will happen. Too seldom does one proceed radically. Such is the early history of many incurable diseases. The paradox is that when the lymphadenopathy is still possibly amenable to complete surgical removal, it is liable to be regarded as benign, whereas when it has become inoperable, one contents oneself by saying that it always has been so.

Certain authors have claimed excellent therapeutic results with Hodgkin's granuloma confined to the gastrointestinal tract, but so far as our experience goes, these patients fare badly, for in no case did a patient survive for more than eighteen months after the initial symptoms, and the average duration of life from onset to death was only nine months. Patients with gastrointestinal lesions incidental to a generalized process similarly appear to have an unfavorable prognosis, if the figures derived from such a small series may be regarded as significant.

The psychologic aspects of treatment should never be overlooked. If the patient is a physician, he should be told the precise diagnosis. The details of the treatment and prognosis need not, and indeed should not, be dwelt on. We have cared for a considerable number of doctors afflicted with Hodgkin's disease or allied conditions, and all but one have borne their disease with cheerful stoicism from beginning to end. In the single exceptional case, serious family difficulties unquestionably contributed to the patient's mental undoing.

If the patient is a layman, it is probably best not to name the disease, even though — as is usually the case — one is asked what it is. Practically all patients are content with evasive answers, and rarely press the point if they are casually told that some lymph nodes are enlarged for some obscure reason and that much can be done to alleviate their symptoms. The mere assurance that symptomatic improvement can be achieved almost always sets the patient's mind at comparative ease, and the initial therapeutic success tends to tide him over subsequent recurrences, even though these may be less amenable to such therapeutic measures as are available. As time passes, the patient himself often comes to the realization that he is going to have the disease the rest of his life, and this recognition gradually changes to an awareness that he is sure to die of the disease. This inner awakening to the bitter truth hurts far less than would a blunt statement on the part of the attendant physician. Less frequently the patient imperceptibly — to himself — grows worse and worse, and he is never genuinely conscious of the impending end. Still less frequently sudden death occurs even when the patient appears to be doing well.

Very rarely one encounters a patient who asks how long he will live, and means it. In such cases an entirely plausible reason is always given for

wishing this exact information. The absence of such a logical reason is usually sufficient evidence that the patient is not truly serious in his questioning. Even so, dogmatism must be avoided, the course of the disease is too erratic. For example, one young man asked how long he would live. From his former physician he had learned the diagnosis. When asked why he wished to know, he replied calmly that he wanted to plan his life in accordance with the prognosis. He was told that he would live for one year, and at his request he was shown the evidence on which this statement was based. "All right," he said, "I will build a house — that takes a year." Six years later, the physician who had made the prognosis received a note in which the patient remarked that the skiing was excellent in the mountains and invited him to come there for the weekend. The patient died four years later following a major surgical operation. The individual patient is not the average patient, and the rules of Hodgkin's disease are made to be broken.

It should be recognized that patients with this disease are unusually quick to grasp the significance of any remark arising from the physician's awareness that the end is approaching, indeed, they exaggerate it. In several of our cases, fear and despair has supplanted hope and a sense of security. For example, a patient who lived in a distant town had done unusually well for five years, but then began to fail, although without realizing it. It was suggested that he get in touch with a local physician so that there might be someone at hand who was familiar with his case. On reaching home he telephoned his son and said, "Well, my death warrant has been signed." In a week he was dead. It may be argued that he would have died anyway, but this is doubtful, and at least he would have died in peace had the subject been brought forward earlier and more tactfully.

In all cases some responsible member of the family, not necessarily the nearest of kin, must be told in lay terms the diagnosis and the probable prognosis. Even here, however, one must be cautious, for as has been repeatedly said, each case is a law unto itself.

#### *Hodgkin's Sarcoma*

The treatment of choice in Hodgkin's sarcoma, as in other forms of Hodgkin's disease, is irradiation, yet it must be admitted that there is no convincing evidence that such treatment, even when given in full doses, is of much avail. Not infrequently, virtually no response is obtained, a result that in Hodgkin's granuloma is extremely rare. In the presence of anemia, transfusions are helpful. The fact that in most cases the condition arises in an internal organ or in the retroperitoneal lymph nodes and is thus less likely than otherwise to be diagnosed at an early stage militates still further against successful therapeutics.

and 3 years after the demonstration by x-ray of a destructive process in the spine involving at least three vertebrae. Early in 1940 there developed considerable pain in the lower back and in both legs, which gradually increased in severity and could be controlled only by opiates. The patient remained cheerful, however, and his physical activities were limited solely by the pain, which became so severe in the fall of 1940 that a dorsal cordotomy was performed. The operation was entirely successful in so far as relieving the pain was concerned, but the patient failed rapidly and died in December, 9 years after the initial symptoms.

In addition to irradiation, three therapeutic adjuncts must be considered: blood transfusions, general care and surgery.

Some authors object to transfusions and believe that they are rarely of benefit and may even be harmful (Wallhauser<sup>5</sup>). We,<sup>1</sup> on the contrary, agree with Gilbert that they are of inestimable value, and it is doubtful whether the reactions to which some authors have drawn attention would occur if careful attention were paid not only to the group but also to the subgroup of both donor and recipient. This is particularly important if repeated transfusions are necessary at rather long intervals, for although, for instance,  $A_1B_2$  blood may produce no reaction on the first transfusion in an  $A_1B_1$  recipient, the patient may gradually build up antibodies against  $B_2$  in such a manner that subsequent transfusions even from the same donor are accompanied by violent reactions.<sup>6</sup> It is our custom to transfuse patients whose red-cell count is 3,000,000 or below unless they are in the terminal stages of the disease. We have never seen an untoward reaction when the bloods were properly matched in both the major and the minor agglutinations.

Iron in the form of ferrous sulfate may be of benefit.

It is obvious that general care is of importance in any chronic condition, and this is no less so in Hodgkin's granuloma. Plenty of rest, ample food that is high in vitamins and the other essential elements, fresh air and sunlight within the tolerance of the patient are all of real value. Not a few patients volunteer the statement that their sense of well-being is greatly enhanced if they stay out-of-doors in the sun.

Obvious foci of infection should be removed, for they undoubtedly have a provocative influence on the condition. For itching, in addition to the irradiation referred to above, local applications of 0.5 per cent phenol in olive oil may be tried. For pain, particularly that arising from bone lesions, salicylates in full doses often produce surprisingly good results. One of our patients had a destructive lesion of the lumbar spine associated with marked pain. X-ray therapy brought about a regression of the bone lesion, but the pain, which was apparently dependent on the resulting scoliosis and muscle spasm, persisted. For several years it has been controlled by large doses — 2 to 6 gm — of aspirin a day, and the patient is able to live a normal and indeed active life.

Our experience with cordotomy for pain has been most unsatisfactory, although there are no doubt cases in which it is of benefit. In 1 case, the skillful injection of the posterior roots with alcohol was followed by complete relief of pain. There was no further discomfort until the patient's death a year later.

The question of surgical intervention is a moot one. First championed by Yates and Bunting in 1917,<sup>7</sup> it has since fallen into disrepute. The great majority of writers on the subject have concluded that it is useless, some because they have seen it fail again and again, others because they have seen the rapid return of lymph nodes in the operative field, and still others because of their belief that Hodgkin's granuloma is always a generalized disease from the start — a belief for which there are no valid grounds. It is true that by the time the patient first seeks medical advice, the process is usually widespread or at least inoperable. It is also true that in many cases the original focus is internal and therefore inaccessible, but both clinical experience and autopsy findings tend to show that the disease begins in one focus and spreads from it — slowly in some cases and rapidly in others.

Gilbert writes: "Surgical procedures have shown themselves useless, they do not influence the evolution of the disease. Local recurrence or extension develops shortly after operation, except in the benign, local and peripheral forms in which the lymph nodes are still movable." Baker and Mann<sup>8</sup> adopt a somewhat more militant and optimistic attitude. They cite the first and second cases in their series, in each of which there was performed surgical excision of the diseased tissues, associated with deep x-ray therapy. The first patient was alive and well thirteen years and the second eleven years after operation. It is the opinion of these authors that when the lymph-node enlargement is localized, surgical excision should be practiced and the area subsequently irradiated. We share this view, with the full recognition that suitable cases are indeed rare and that even in them some hidden focus not apparent at the time of operation may frustrate attempts at cure. Much has been said and written about the necessity for early diagnosis in cancer, and it is generally appreciated that in early recognition of this disease lies the best hope of true cure. The same can be said for Hodgkin's granuloma.

Two of our patients with this disease have been subjected to radical excision of cervical lymph nodes. One was alive and free from signs and symptoms of disease ten years after operation, and the other is alive and well seven years after operation. Both patients were children. It is obvious that in view of the extremely variable course of the disease, no conclusions can be drawn from these cases, and at best the results are only suggestive. Too often, however, one hesitates, argues and procrastinates.

ur patients died in less than six months after the pparent onset, and 11 survived for eight years or more, 7 of these being alive and in reasonably good health for eight to twenty-two years after the first symptom

If these two groups of cases, examples of the prognostic extremes, are contrasted, certain definite points stand out. The onset in the rapidly fatal cases was usually suggestive of an acute infection or indicated internal involvement. Chills, dyspnea, cough, fever, abdominal pain, sweating and dysphagia were seen at the very beginning of the disease, and only 7 of the 15 patients had palpable superficial lymph nodes when first seen, although all but two had peripheral lymphadenopathy prior to death (Table 6). In almost all cases in which cough,

TABLE 6 Most Frequent Initial Symptoms in Fifteen Rapidly Fatal Cases of Hodgkin's Granuloma

SYMPTOM	NO OF CASES
Cough	9
Dyspnea	7
Superficial lymphadenopathy	7
Chills	5
Hemoptysis	2
Fever	2
Dysphagia	1
Sweats	1

dyspnea, chills, sweats and fever were present at the onset of the disease, death occurred within six months. One cannot of course expect this rule to hold in every case, but it appears to be a helpful prognostic guide. As Uddström<sup>9</sup> points out, however, the disease process may have been in existence much longer than the symptoms indicate when it has its origin in the hilar, mesenteric or retroperitoneal lymph nodes, and the actual duration of the disease may therefore be longer than is evidenced by the available clinical data.

Of the 11 patients who survived for eight years or longer, and 8 of whom are now alive and in reasonably good health, 8 sought medical advice for simple, painless localized lymphadenopathy without any associated signs or symptoms. One had in addition a certain amount of general fatigue, 1 complained of dyspnea, and 1 entered the hospital for the first time with a complaint of weakness of the legs.

The contrast between these two groups is sufficiently arresting to demand attention. By and large, in the rapidly fatal cases there was an onset suggestive of an acute infection, whereas in those of long duration the patients presented themselves with simple lymphadenopathy, only occasionally associated with symptoms of generalized disease. The more nearly a given case approaches one or another of the extremes, the more does the course run true to form.

Most students of this subject agree that no definite relation exists between the onset of pulmonary findings and the progress of the disease. Falconer

and Leonard<sup>10</sup> were unable to determine any connection between the time of onset of pulmonary symptoms and the time of death. It appears, however, that these authors dated the onset of pulmonary involvement from the first pulmonary symptoms, which may well have been due to mediastinal or hilar node involvement rather than to actual implication of the parenchyma. Similarly, Pierce et al.<sup>11</sup> state that the roentgenological appearance offers no criteria for prognosis.

Our own experience has been somewhat more definitive. No patient in whom pulmonary lesions were demonstrated at autopsy lived for more than eight months after these changes had been discovered during life, and the great majority died within three months. Three patients who gave x-ray evidence of pulmonary invasion from mediastinal or hilar nodes survived for over two years after the demonstration of these changes, but in no case was there autopsy confirmation of the reported pulmonary involvement. It is perhaps of some interest that all 3 of these patients had an unusually long course, averaging over eight years. No definite conclusions can therefore be drawn, but it seems probable that involvement of the lung parenchyma is associated in many cases with rapidly advancing disease.

Ziegler<sup>12</sup> concluded that Hodgkin's disease runs a more rapid course in children than in older patients. Uddström<sup>9</sup> believed the reverse to be true. Our own experience is that age alone has little or no influence on the prognosis.

That the disease may run an extremely rapid course has been already pointed out. For example a six-year-old girl was noted by her parents to have enlarged lymph nodes in each side of the neck in December, 1933, and one week later developed cough and fever. She died of respiratory failure on January 10, 1934, within six weeks of onset.

In sharp contrast is the following case.

A P., a 10-year-old boy, in 1915 developed a painless lump in the left side of the neck. It gradually increased in size until November, 1917, when it was removed by surgery. Histologic examination of the node showed the typical picture of Hodgkin's granuloma (MGH-S17-11-58).

On admission to the hospital on December 17, 1917, physical examination was entirely normal except for the presence of several firm lymph nodes, varying from 0.5 to 1.0 cm. in diameter in the anterior triangle of the right side of the neck. No lymph nodes were palpable in any other area. The red-cell, white-cell and differential counts were essentially normal.

Between December 27 and May 31, 1918, a total of 6100 mc. hr. of radium (2 mm. of lead and 2 cm. of gauze screening) was given to the left side of the neck and the left axilla, although there were no palpable lymph nodes in the latter area. The cervical lymph nodes disappeared, and the patient was not seen again until December 20, 1924. At that time he was in excellent condition, and the physical examination was entirely within normal limits.

He returned on August 22, 1930, when a 2-cm. node was found under the left jaw. There were many carious teeth in the lower jaw. The node was removed on September 6. The microscopic diagnosis was Hodgkin's granuloma. A full suberythema dose of x-ray was given at 250 kilovolts over the left side of the neck.

Since that time the patient has remained entirely well. When last seen in December, 1939, 22 years after onset,

If the condition is discovered at an early stage, when the lesion is comparatively localized, radical surgical intervention appears to be indicated, but we have not encountered any such case

### PROGNOSIS

#### *Hodgkin's Paragranuloma*

For certain forms of malignant disease, such as osteogenic sarcoma, a maximal time of survival may be set with some degree of accuracy, and in the great majority of cases the physician may rest assured that an actual cure has been effected if the patient survives this date. This situation does not obtain in Hodgkin's paragranuloma.

The prognosis of this disease is comparatively good. Of 26 patients followed to date, 14 (54 per cent) have been alive and free from symptoms for five years or more, and 5 have survived a fifteen-year period (Table 1). It is of considerable sig-

TABLE 1 *Survival Period in Cases of Hodgkin's Paragranuloma*

TYPE OF CASE	SURVIVAL TO DATE OR TO DEATH	NO OF CASES
	yr	
Patient alive	Less than 3	0
	3-9	7
	10-24	6
	25 or more	1
Patient dead	Less than 3	5*
	3-9	6†
	10 or more	1
Total		26

\*Death due to unrelated causes in 3 cases

†Death due to unrelated causes in 2 cases

nificance that of the 12 patients who have died, 5 succumbed to diseases entirely unrelated to their disease, the remainder developed Hodgkin's granuloma and died in less than ten years after onset.

#### *Hodgkin's Granuloma*

Hodgkin's granuloma is usually regarded as a fatal condition, leading to death in one to three years. In general such is the case, yet it is important to remember that the individual patient is not the average one, that the span of life from onset

TABLE 2 *Average Duration of Disease from Onset to Death according to Age at Onset in Cases of Hodgkin's Granuloma*

AGE AT ONSET	MEDIAN DURATION	NO OF CASES
yr	yr	
Less than 10	2.5	14
10-19	2.4	26
20-29	2.8	21
30-39	2.4	19
40-49	1.3	23
50-59	2.6	18
60-69	0.6	12
70-79	0.9	2
80-89	0.7	1
Total		136

varies within wide limits, and that rarely a patient survives without evidence of active disease for so long a time that an actual cure may be considered at least possible.

In Table 2 is shown the duration of life from the first sign or symptom that could properly be con-

sidered as due to the disease itself in the 136 cases of our series in which the patients died of the disease after being followed throughout its course. Three patients died of entirely unrelated causes and are therefore not included. It is apparent that the average length of life from onset to death is approximately two and a half years. Uddström's<sup>1</sup> data, based in a like manner on 494 fatal cases, are

TABLE 3 *Duration of Disease from Onset to Death in Cases of Hodgkin's Granuloma*

DURATION	PRESENT SERIES (136 CASES)	UDDSTRÖM'S SERIES (494 CASES)
yr	%	%
Less than 1	24	33
1-2	45	45
3-4	17	16
5-9	13	6
10 or more	1	0

in essential agreement with ours, and Wallhauser,<sup>2</sup> from a review of the literature, has come to essentially the same conclusions. These average figures, however, by no means tell the whole story. Thirteen per cent of our patients lived for five years or more after onset, and 1 died eleven years after onset (Table 3). About 30 per cent, therefore, lived definitely longer than either those in the average or median group, and 13 per cent lived twice as long.

When one considers those patients who were still alive, a somewhat different picture is seen (Tables 4 and 5). It is apparent that the duration of the

TABLE 4 *Average Duration of Disease from Onset to Date according to Age at Onset in Cases of Hodgkin's Granuloma*

AGE AT ONSET	MEDIAN DURATION	NO OF CASES
yr	yr	
Less than 10	5.0	5
10-19	6.0	3
20-29	5.6	9
30-39	4.3	4
40-49	5.7	6
50-59	4.8	6
60-69	3.0	1
70-79	5.2	1
Total		35

disease in the patients in both series is notably longer than it was in those who died. Whether this is due to the statistical error of a relatively small

TABLE 5 *Duration of Disease from Onset to Date in Cases of Hodgkin's Granuloma*

PERIOD	PRESENT SERIES (35 CASES)	UDDSTRÖM'S SERIES (34 CASES)
yr	%	%
Less than 3	22	9
3-4	28	47
5-9	44	38
10 or more	6	6

series — 69 living cases — or can be attributed to the increased efficacy of more recent x-ray therapy is a question that cannot be answered with any degree of assurance. The fact remains, however, that of these 69 patients, 28 (40 per cent) had had their disease for five years or more and that an additional 6 per cent had survived a ten-year period.

The question therefore naturally arises whether at the onset there are any criteria by which one can foretell the course of the disease. Fifteen of

## THE WOLFF-PARKINSON-WHITE SYNDROME

CAPTAIN NORMAN H BOYER, M C , A U S \*

**T**O THOSE with extensive electrocardiographic experience, especially if it includes a large proportion of young adults, the finding of the pattern of a short PR interval and a prolonged QRS complex comes as no great surprise. That it is not a rare occurrence, as might be concluded from the many papers in the literature reporting one or two cases, needs to be emphasized, because this combination is still all too frequently misinterpreted as being of clinical significance. Such misinterpretation might be considered negligible if the electrocardiographic findings occurred but rarely. On the other hand, if the pattern is as frequent as experience indicates, it becomes important, particularly in the military service that it receive wider publicity.

During the routine interpretation of electrocardiograms in an Army general hospital, this curious pattern seemed to appear with greater frequency than had been expected. Accordingly, the last 2000 electrocardiograms were reviewed. The pattern of a short PR interval and a prolonged QRS complex was encountered at one time or other in 7 cases. Since the records represented 1356 patients, the incidence was 0.5 per cent. At the present strength of the armed forces this is equivalent to about four divisions. If even a small percentage of such men were to be returned from combat areas with diagnoses of bundle-branch block, a considerable loss of manpower would result. Furthermore, even when such a record is later accurately evaluated in another hospital, it is difficult and often impossible to salvage the patient because of a firmly entrenched cardiac neurosis or neurocirculatory asthenia. Moreover, when and if these patients are returned to civilian life, they will probably remain partially ineffective.

Brief summaries of these cases follow, together with an illustrative electrocardiogram.

**CASE 1** A 19-year-old soldier was admitted to the hospital because of recurrent episodes of dizziness, shortness of breath, palpitation and occasional fainting. These symptoms had been present since infancy and were usually brought on by exertion. Early in life the patient had been cautioned about his heart because of a murmur. He was admitted to an overseas hospital, where a precordial systolic murmur was heard, and was evacuated with a diagnosis of interventricular septal defect and bundle-branch block.

Examination revealed an inconsequential precordial systolic murmur and an electrocardiographic pattern of a short PR interval and a prolonged QRS complex. The patient was made to exercise to the point of shortness of breath and dizziness, without any change in the blood pressure, cardiac rhythm or electrocardiographic pattern. The intravenous injection of 2 mg of atropine sulfate also failed to alter the electrocardiogram. Fluoroscopic examination of the heart revealed no abnormalities. The patient was considered to have severe neurocirculatory asthenia.

**CASE 2** A 34-year-old soldier entered the hospital because of attacks of paroxysmal tachycardia, which had begun 5

years previously. Between attacks he had been symptom-free. Physical and roentgenographic examinations were normal. Electrocardiograms consistently showed a short PR interval and a prolonged QRS complex, which were unaffected by atropine.

**CASE 3** A 34-year-old soldier was admitted on his return from overseas with a diagnosis of rheumatic fever. He had had a probable attack of rheumatic fever at the age of 4 and an authenticated attack in an Army hospital in September 1943. He was discharged back to duty and fared well until June 1944, when he had a recurrence of joint pain, with fever and an elevated erythrocytic sedimentation rate. Several electrocardiograms were said to have revealed intraventricular conduction defect. The patient was evacuated to the United States and on arrival had no complaints.

The physical examination was normal. Review of the previous electrocardiograms showed the pattern of a short PR interval and a prolonged QRS complex, but the record obtained on admission was normal save for a single beat, which was at first interpreted as a late ventricular ectopic beat. A review of the previous records made it apparent, however, that this beat was identical with the complexes previously present. Following the subcutaneous administration of 1 mg of physostigmine the pattern was reproduced in all cycles. There was no clinical or laboratory evidence of active rheumatic fever or of organic heart disease.

**CASE 4** A 25-year-old soldier with a history of possible rheumatic fever at the age of 12 was admitted to an overseas hospital because of multiple-joint pain, without objective swelling, redness or local heat. There was no fever, leukocytosis, or elevation of the erythrocytic sedimentation rate. Electrocardiograms, however, were interpreted as showing left bundle-branch block. Largely on the basis of the latter report the patient was considered as having active rheumatic infection and was evacuated to the United States.

On admission there were multiple complaints including fleeting joint pain, precordial pain, palpitation and shortness of breath. Physical, laboratory and roentgen-ray examinations were normal. Electrocardiograms, which were identical with previous records, showed the pattern of a short PR interval and a prolonged QRS complex. The patient was considered to have a psychoneurosis, including neurocirculatory asthenia and psychogenic "rheumatism." The electrocardiogram is reproduced in Figure 1.

**CASE 5** The clinical record was not available in this case, but the final diagnosis was severe neurocirculatory asthenia.

**CASE 6** A 30-year-old soldier was seen because of attacks of paroxysmal tachycardia for the last 4 years. In the intervals between attacks he was essentially symptom-free. Physical and roentgen-ray examinations of the heart were normal. The electrocardiogram showed a short PR interval and a prolonged QRS complex.

**CASE 7** A 33-year-old soldier was referred for an electrocardiogram before shock therapy for catatonic schizophrenia. Although a history of sharp precordial pain and shortness of breath was obtained, the patients had no complaints and answered all leading questions in the affirmative. The history was accordingly discounted. Physical and roentgen-ray examinations of the heart were normal. The electrocardiogram revealed a short PR interval and a prolonged QRS complex. Shock therapy was not employed because of an erroneous diagnosis of bundle-branch block.

## DISCUSSION

The mechanism of this curious electrocardiographic pattern, first clearly defined by Wolff, Parkinson and White,<sup>1</sup> still remains unexplained. The theory of a short-circuiting bundle between the auricles and ventricles, proposed by Wolferth and Wood,<sup>2</sup> has been almost universally accepted by recent authors. The demonstration by Butterworth and Pindexter<sup>3,4</sup> that the pattern can be

\*Assistant professor of medicine, Boston University School of Medicine, and assistant physician, Evans Memorial Massachusetts Memorial Hospital (on leave of absence).

he was free from symptoms and physical examination disclosed no abnormalities

Between the extremes of these two cases lie the majority of cases. It is well to bear in mind that it is often difficult to predict the course with any degree of accuracy. That such is indeed the fact is well illustrated by a case in which the patient had at onset symptoms of a generalized disease and signs of involvement not only of lymph nodes but of bone, but was alive and at work twelve years later.

Rarely sudden death occurs. MacCallum<sup>13</sup> describes a case in which the patient leaned forward to drink a cup of tea and died instantly. Autopsy showed that the odontoid process of the axis had been completely destroyed by the disease and that the slight effort of motion had dislocated the spinal column so as practically to cut the cord in two. One of our patients, a boy of fifteen, was eating his luncheon in comparative comfort. In the midst of the meal, he sighed, laid down his knife and fork and expired. Permission for an autopsy was not obtained. As Wallhauser<sup>5</sup> points out, the manner and time of death depend on several variable factors, chiefly the course, — acute or chronic, — the organs and situations involved, the degree of anemia, secondary infections, the quality of the patient's resistance and the treatment. The importance of the last two factors is too frequently overlooked.

It is difficult to evaluate the prognostic significance of bone lesions in Hodgkin's disease. Many patients in our series so affected died within less than one and a half years of x-ray discovery of the lesion and 63 per cent died within less than a year after it. A patient with a massive erosion of the sternum, however, was in seemingly good health and hard at work twelve years after its discovery, and of the patients who died within a year of the demonstration of the bone lesion, 33 per cent had already had unequivocal signs of Hodgkin's disease elsewhere for three years or more. From the available evidence it does not appear that bone lesions materially alter the outlook. In this opinion Uehlinger<sup>14</sup> concurs.

### Hodgkin's Sarcoma

None of our patients with Hodgkin's sarcoma lived for more than three years after onset, and nearly 60 per cent died within two years (Table 7).

TABLE 7 Duration of Disease from Onset to Death in Cases of Hodgkin's Sarcoma

DURATION	No. OF CASES
mo	
1-6	12
7-12	6
13-24	13
25-36	1
Total	32

Again one sees the sharp contrast between Hodgkin's sarcoma and Hodgkin's granuloma. In our experience, the former is invariably fatal within a comparatively short period of time, whereas the latter usually runs a relatively benign course and in rare cases is actually cured.

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intrinsic deflection is delayed for 0.11 second in the ectopic beat, as compared with 0.04 second in the normal beats. The available material has not allowed exhaustive study of precordial leads, but at present it is fair to say that the chest leads in the

1 had schizophrenia, possibly with neurocirculatory asthenia. That the relatively high incidence of neurocirculatory asthenia is not explainable on the basis that it is such patients who, in this age group, are likeliest to have electrocardiograms made is attested by the fact that by far the majority of the 2000 records reviewed were made in patients in various stages of rheumatic fever. Only one patient (Case 3) was in the latter group, and he had no symptoms whatever.

Two explanations of the association of this electrocardiographic pattern and neurocirculatory asthenia are plausible. First, the deranged nervous system may actually produce the pattern. This theory is supported by the frequent, although by no means invariable, alteration from abnormal to normal or from normal to abnormal patterns induced by drugs known to act on the vegetative nervous system. Second, the abnormal sequence of excitation may result in cardiac sensations that, in certain susceptible persons, may lead to "heart consciousness," neurocirculatory asthenia or cardiac neurosis. Although the diagnosis of organic heart disease made on the basis of the electrocardiogram undoubtedly contributed to an increase in symptoms in the present group, it was not the cause of the symptoms of neurocirculatory asthenia, for the complaints in all the patients in whom this diagnosis has been made were present before the electrocardiogram was obtained.

The recent report of sudden death in a patient who had previously shown the Wolff-Parkinson-White pattern<sup>5</sup> should not lead to undue emphasis on the possibility of such a disaster. The rarity of sudden death in young persons without clear pathologic entities and the apparent frequency of the abnormal electrocardiographic pattern warrant accepting a slight risk, if such exists, to avoid creating or adding to anxiety states.

#### SUMMARY

The electrocardiographic pattern of a short PR interval and a prolonged QRS complex has been encountered rather frequently in an Army general hospital, the incidence being 0.5 per cent of patients in whom electrocardiograms were made. Several of these patients had been unnecessarily evacuated from combat areas.

Provided that this experience is not unique, it seems likely that many more soldiers will be unnecessarily evacuated unless those responsible for electrocardiographic interpretations familiarize themselves with the pattern and recognize its probable benignity. The frequency of psychoneurosis in the present series of patients was high, and particularly in such patients it is desirable to avoid adding to their symptoms with a diagnosis of bundle-branch block or myocardial damage.

The mechanism of this pattern is still unexplained. The theory of aberrant conduction tissue between

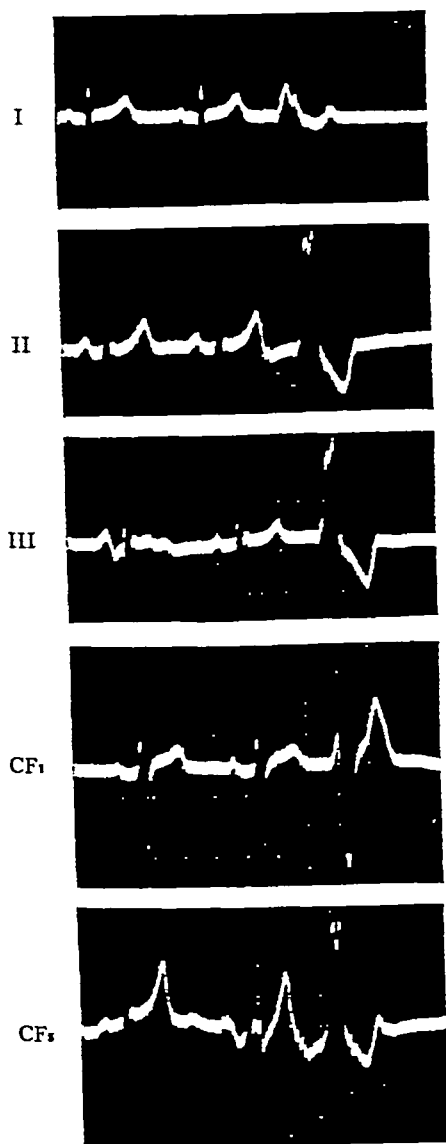


FIGURE 2 Electrocardiogram Showing Trigeminal Rhythm Due to Regularly Recurring Ventricular Ectopic Beats. Note that the onset of the intrinsic deflection in the ectopic beats varies with the position of the precordial electrode, as it does in bundle-branch block.

Wolff-Parkinson-White pattern do not resemble those from either ventricular ectopic beats or bundle-branch block.

In the first clear clinical description of this pattern, that by Wolff, Parkinson and White<sup>1</sup> it was said to be usually associated with paroxysmal tachycardia. In the present series only 2 patients had clear-cut paroxysmal tachycardia, 1 had no symptoms, 3 had neurocirculatory asthenia, and



reproduced in animals by the artificial introduction of such a short circuit attests to the logic of the theory, but neither this experimental work nor the histologic demonstration of an auriculoventricular band in such a case by Wood, Wolferth, and Geckeler<sup>5</sup> absolutely establishes the mechanism.

There are several features of this syndrome that are not satisfactorily explained by the theory of an

from the right and the left precordial position. This feature distinguishes the precordial lead pattern from that of bundle-branch block, in which the interval between the onset of the QRS complex and the intrinsic deflection is prolonged over the blocked ventricle but is normal over the unblocked ventricle. Equal blocking over both ventricular areas, as seen in Figure 1, offers a serious objection to the theory

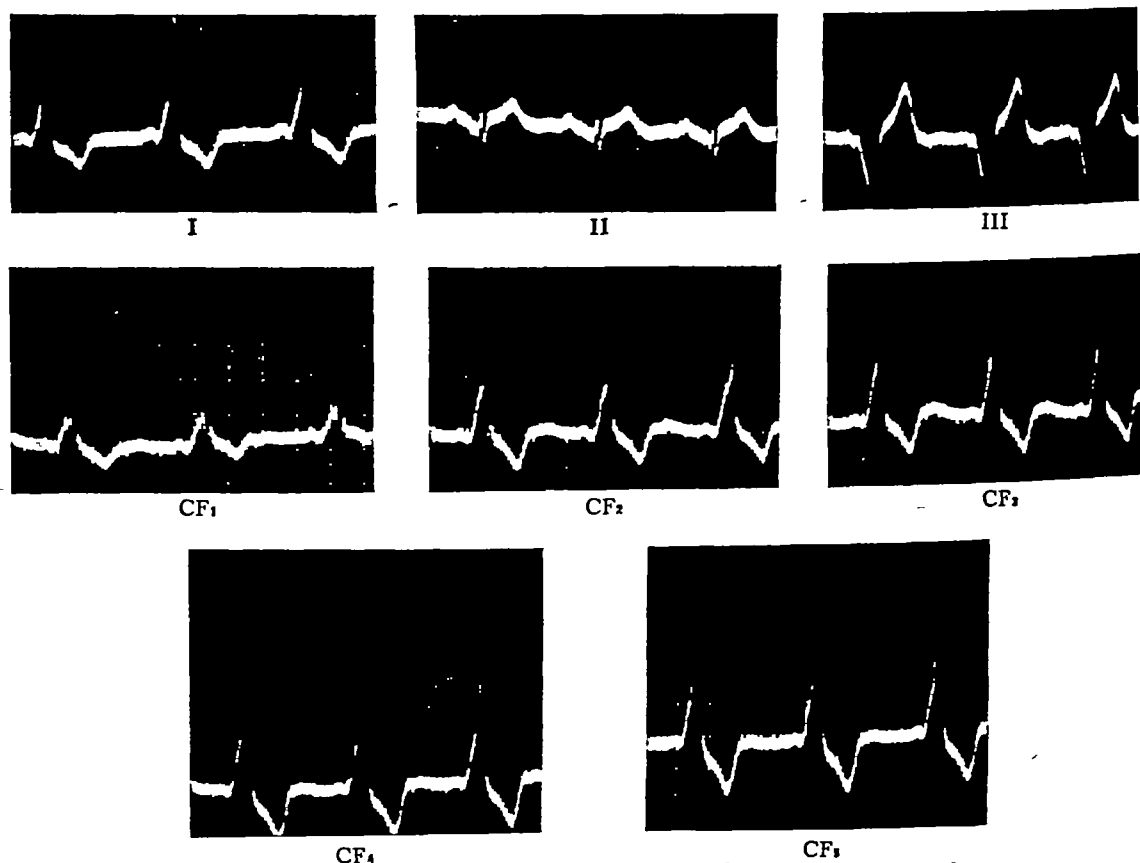


FIGURE 1 Electrocardiogram in Case 4

*Note that the onset of the intrinsic deflection is equally delayed in all precordial leads*

accessory auriculoventricular band. For example, the pattern apparently disappears with advancing age, yet vagal tone increases rather than decreases with age. Inasmuch as an increase in vagal tone may reproduce the pattern when the electrocardiogram is normal, as in Case 3, and a decrease in vagal tone produced by exercise or atropine may temporarily abolish it, it is curious that it is not more frequent in older people. Regular disappearance of the anatomic structure after a certain age seems unlikely.

A somewhat more important objection to the theory of an accessory band is to be found in the failure of multiple precordial leads to establish early excitation of one or the other ventricle. Figure 1 shows a series of CF leads in Case 4. It may be seen that the interval from the beginning of QRS complex to the onset of the intrinsic deflection—that is, the first rapid downward movement of the string—is the same—about 0.08 second—in leads taken

of abnormally early excitation of one of the ventricles.

The spread of impulses over the ventricles, if activation occurs by way of an accessory pathway, may logically be considered more comparable to ventricular ectopic beats than to bundle-branch block. The literature immediately available contained no information on the pattern of precordial leads during ventricular ectopic beats. Accordingly, multiple chest leads were obtained in patients with frequent ventricular ectopic beats. The result in one such case—that of a twenty-five-year-old Negro with trigeminal rhythm but no detectable heart disease—is shown in Figure 2. It may be seen that the pattern is the same as in left bundle-branch block. Over the right ventricle the onset of the intrinsic deflection in the ectopic beat is delayed for only 0.04 second—0.02 second more than for the normal beats in the same area. Over the left side of the precordium the onset of the in-

was available at all times in the bleeding room. In addition, all donors with syncope were seen by the medical officer in charge, and in each case a report stating the time of onset and giving various other data pertaining to the reaction was immediately made out. The pulse and blood pressure were taken at five-minute intervals and recorded until normal levels were obtained.

### CLASSIFICATION OF SYNCOPE

Syncope is a transient form of vasomotor collapse that has certain characteristic symptoms and signs. Although various classifications have been proposed for syncope in blood donors,<sup>3</sup> reactions that did not require additional rest were disregarded in this study. Those in which there occurred loss of consciousness or convulsive manifestations were arbitrarily classified as severe syncope, otherwise the case was classified as mild syncope. In this manner 162 cases of syncope were encountered in the first series, 17 of which were severe, and 527 cases in the second series, 158 of which were severe.

On the basis of this experience an attempt has been made to present the clinical findings and to discuss the constitutional and contributory factors in syncope. Since the 158 cases of severe syncope in the second series were the best defined and most accurately controlled, more detailed observations are presented in regard to them than in regard to those in the first series.

### CLINICAL MANIFESTATIONS

The symptoms and signs of syncope encountered in this study were similar to those described in blood donors by Brown and McCormack.<sup>4</sup>

#### Symptoms

Syncope often developed without warning, but some donors complained of weakness or dizziness, and at times restlessness, yawning or sighing occurred. Rarely a definite aura was present. The most frequent symptom with the attack in the 158 severe cases in the second series was a feeling

TABLE 1 Physical Signs of Severe Syncope

PHYSICAL SIGN	PERCENTAGES
Pallor	99
Loss of consciousness	95
Fall in pulse	83
Fall in blood pressure	77
Sweating	65
Dilated pupils	38
Generalized convulsions	28
Vomiting	7
Loss of sphincter control	6
Hyperventilation	5
Tetany	4

of warmth, which occurred in 63 per cent. Epigastric distress (32 per cent) and nausea (32 per cent) were also present but were usually mild in degree. In addition, there were a variety of other less frequent complaints, such as spots before the eyes, blindness, tinnitus, urgency to void or defecate and numbness and tingling in the hands.

#### Signs

The nature and frequency of the various physical signs of severe syncope are shown in Table 1.

**Pallor** This was the most frequent sign and was usually marked. At times the skin showed a cyanotic tinge, and in some of the more profound cases the patient gave the appearance of impending death.

**Loss of consciousness** The onset was usually abrupt. Most donors remained unconscious for only a few seconds, but in some unconsciousness was more prolonged. Consciousness was generally recovered suddenly, and there was amnesia for the event.

**Fall in pulse** Of the 158 donors with severe syncope, 83 per cent had a pulse of 60 or lower. In a control group 45 per cent of donors had a pulse of 60 or below after bleeding. In cases of extremely severe syncope the pulse was frequently imperceptible or very slow.

**Fall in blood pressure** Seventy-seven per cent of the donors with severe syncope had a drop in systolic blood pressure of 30 or more, compared with 1 per cent in a control group. There was always a concomitant and corresponding drop in the diastolic pressure. The lowest blood-pressure level was usually the initial one, and this did not necessarily occur during the period of unconsciousness. The blood pressure generally rose during the recovery period, which in most cases was half an hour or less, but occasionally the low blood pressure persisted for hours.

**Sweating** This was a frequent finding. Drenching perspiration was observed more frequently in men, especially in those with profound syncope. Sweating occurred all over the body, but unlike this sign in traumatic shock, the skin was usually warm rather than cold.

**Dilatation of pupils** Pupillary changes were found in over a third of the cases of severe syncope. These were of variable degree and often so transient that they may have been missed in some patients. Occasionally the pupils were constricted, but no definite correlation between either type of pupillary changes and the degree of syncope was noted.

**Generalized convulsions** In donors who had convulsive seizures the onset was almost always abrupt. A tonic spasm was usually present throughout the body, and frequently the head and eyes deviated to one side, with the back arched in opisthotonos. The pupils were generally dilated and momentarily fixed. In some cases there were clonic movements of the extremities, followed by a period of snorting, stertorous respiration. The face was usually flushed and occasionally slightly cyanotic. The blood pressure during the attack was normal or slightly elevated. Immediately afterward in some donors a drop in blood pressure and pulse was observed, but in others there was no fall in blood pressure or pulse, either during or after a

the auricle and ventricle does not satisfactorily account for some of the characteristics of the syndrome. In particular, it does not seem to explain observations made with multiple chest leads.

Since this manuscript was submitted, a comprehensive study of precordial, thoracic and esophageal leads in the Wolff-Parkinson-White syndrome has been reported by Rosenbaum et al.<sup>6</sup> They suggest that when the anomalous pattern is present, conduction occurs by way of both the normal conduction pathways and one or more accessory pathways. Although this suggestion helps to explain the pattern better than does the theory of aberrant spread throughout the ventricles, the hypothesis rests on a good deal of speculation. It is logical speculation, however, and tempts one to conjecture that the premature excitation involves a particular muscle bundle—probably one of the deeper ones. The reasons for such a conjecture are as follows. First, the magnitude of the premature component of the QRS complex suggests that a sizable bulk of muscle is involved. Second, if one assumes that the onset of the intrinsic deflection signals the arrival of the impulse at the epicardial surface underlying the electrode, it follows from the study of unipolar leads

that the premature excitation does not reach the epicardial surface at any point that can be reached by indirect unipolar leads.

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## SYNCOPE IN BLOOD DONORS

MAJOR WILLIAM C. MOLONEY, M.C., A.U.S.,\* CAPTAIN LELIAS R. LONNERGAN, M.C., A.U.S.  
AND MAJOR JAMES K. MCCLINTOCK, M.C., A.U.S.

THE present emergency has provided an unusually abundant opportunity for the study of syncope, or fainting, in blood donors. Although not in itself serious, fainting results in loss of time to the donor, it is detrimental to the efficiency of the donor center, and, as pointed out by Taylor,<sup>1</sup> an occasional donor has fallen and suffered injury. The present investigation of some of the clinical and etiologic aspects of syncope was undertaken to aid in reducing the incidence of fainting in blood donors. Aside from practical considerations, it is hoped that the observations and data recorded in this paper will shed some light on the pathogenesis of the complex and interesting problem of syncope, about which, as McDowell<sup>2</sup> has recently stated, there exists a great deal of confusion.

## MATERIAL AND METHODS

This study concerns two series of blood donors bled under different circumstances and therefore offering some interesting comparative data. The first series consisted of 6882 donors—2202 men and 4680 women—who were bled between May, 1942, and March, 1943. The blood was obtained at the Atlanta Red Cross Blood Donor Center under the direction of the Blood Research and Plasma Laboratory of the United States Army. Physically fit donors were selected on a basis similar to that of the present Red Cross requirements, with certain important variations. A donation could be either 250 or 500 cc, but no 500-cc donations

were taken from persons under twenty-one years of age or weighing less than 150 pounds. If a donor was nervous or if other reasons seemed to warrant it, only 250 cc was taken even if the donor was within the weight and age limits of the larger donation. All the bleedings were done by the staff of physicians assigned to the center, and a closed-vacuum-bottle method was employed. The donations amounted to only thirty to seventy a day, so that it was possible to adopt an unhurried attitude and to permit the donor to rest for ten or fifteen minutes on the bleeding bed after the donation. The second series consisted of 9251 donors—3917 men and 5334 women. Bleedings were taken from March 8 to June 1, 1943. This program was carried out according to the methods and technics recommended for use in Red Cross blood procurement centers.<sup>1</sup> All accepted donors weighing 110 pounds or over gave 500 cc of blood, unless, as in exceptional cases, the bleeding had to be stopped before this amount was obtained. The technics of the preparation of the arm and the venipuncture were the same in both series, but in the second series the standard Red Cross bleeding set<sup>1</sup> was used, and practically all the bleedings were done by specially trained graduate nurses. One or two staff physicians were in charge of the bleeding room at all times. Of necessity, the atmosphere was somewhat more impersonal than in the first series, moreover, the rest after bleeding was shortened to five minutes unless otherwise indicated.

The personnel was instructed regarding the early signs and symptoms of syncope, and a trained nurse especially designated as the "reaction nurse"

\*Assistant professor of clinical medicine, Tufts College Medical School, and visiting physician, Carney Hospital and St. Elizabeth's Hospital (on leave of absence).

hardly significant figure. In the present study the surface area of donors in severe syncope differed little from that of controls, this was true of both sexes (Table 2).

In experiments with professional donors, Ebert, Stead and Gibson<sup>9</sup> found that if 15 to 20 per cent of the normal blood volume was removed collapse

TABLE 2 Surface Area and Blood Volume in Control Donors and Those with Severe Syncope

DONORS	SEX	NO OF DONORS	AVERAGE SURFACE AREA	AVERAGE BLOOD VOLUME
			sq m	cc
Control donors	F	114	1.66	4980
	M	78	1.91	5750
Donors with severe syncope*	F	88	1.65	4950
	M	67	1.86	5580

\*Three cases omitted because of incomplete data

usually ensued and that this state had all the features of syncope. These authors also emphasized the role of psychic and reflex factors in collapse. In obtaining blood under the conditions outlined in this paper, however, even the donor with the smallest blood volume did not lose more than 12 per cent of his blood. Nevertheless, it seems logical to assume that a person deprived of a relatively greater percentage of blood will be less capable of adjusting the circulatory mechanism in the presence of reflex vasomotor change than those deprived of smaller amounts.

**Environment** The importance of the surroundings and the attitude of the staff in the donor center has been emphasized by Williams<sup>10</sup> and Taylor.<sup>1</sup> Undoubtedly in this study the more favorable circumstances under which the first series of donors was bled contributed materially in lessening the syncope rate as compared with that in the second series.

**Occupation** Fatigue, lack of sleep and dehydration due to heavy or prolonged occupations are no doubt factors in syncope.<sup>8</sup> Such conditions were not encountered in this study. Greenbury<sup>3</sup> found that young female clerical workers fainted oftener

TABLE 3 Contributory Factors in Severe Syncope

FACTOR	CONTROL DONORS	PERCENTAGE DONORS WITH SEVERE SYNCOPE
History of fainting	16	50
Nervousness	23	49
Fatigue	15	33
Fasting for over five hours	53	65
Pain from venipuncture	7	11
Donation		
First	64	67
Second	22	11
Third or higher	14	3

than did those in other occupations, but he did not take into account age and other factors, which appear to have much more bearing on the problem than does occupation.

**Weather** It is a widespread belief that fainting occurs with special frequency in a warm atmosphere, but studies by various authors tend to discount

the influence of high humidity and temperature. An investigation of these factors was carried out in this study. Although no close correlation was evident, the impression gained from clinical experience that heat and humidity contribute to higher syncope rates persists.

### CONTRIBUTORY FACTORS

In addition to the constitutional and general factors, there are a number of important contributory factors in syncope. Some of these are shown in Table 3, which is a comparison of a group of 200 control donors with those in the second series who had severe syncope. An outstanding fact was the high incidence of a prior history of fainting in the syncope group as compared with that in the controls. It is also apparent that nervousness and fatigue play important roles in conditioning a person to fainting. Since fasting was common to both groups, it is difficult to evaluate. Lawrence and Plaut<sup>11</sup> found no significant difference in blood-sugar levels between fainters and non-fainters, and hypoglycemia probably does not enter into the picture. Pain is a relatively infrequent complaint owing to the use of local anesthesia and skillful venipuncture, and hence has not been a significant factor in syncope.

When severe syncope occurred on the first donation, the donor was not called back for further donations. Nevertheless, since nervousness and apprehension are much more evident on the first visit to the donor center than at later ones, the high incidence of severe syncope on this occasion as compared with the much less frequent occurrence on subsequent donations is understandable.

**Epidemic Fainting**<sup>12</sup> This phenomenon was encountered not infrequently in young donors. These persons, usually from the same office or service group, would "talk each other into a faint." Promptly placing the donor in a supine position almost always resulted in a mild type of syncope, the *forme fruste* of Weiss.<sup>12</sup> Epidemic fainting is excellent evidence of the strong psychologic effect of suggestion.

**Postural Factors** As pointed out by Weiss,<sup>12</sup> syncope usually occurs in the upright position. Nevertheless, in these blood donors severe syncope frequently developed in the supine position. This finding must be qualified by the fact that some delayed faintings were not reported, especially if the donor had left the center. Second, in a number of patients with mild or incipient syncope this would have undoubtedly become severe if they had been allowed to get up before the circulatory system had become adjusted. It is evident that a change in posture may bring about increased cerebral ischemia and act as a contributory factor to precipitate syncope.

### DISCUSSION

The clinical features of syncope as observed in this study were quite similar to those described by

convulsion All these donors were apparently unconscious during the seizure, but none of them bit their tongues or sustained any significant injury, even with violent convulsions

**Vomiting** Although relatively infrequent, vomiting was occasionally severe and profuse Many donors felt relieved after it, but in some cases nausea and epigastric distress persisted for hours Vomiting may be an outstanding feature of otherwise mild cases of syncope

**Loss of sphincter control** Although of rare occurrence, urinary incontinence was observed, especially in young women It was invariably associated with deep syncope and often occurred during or just following a convulsive seizure Loss of bowel control was not observed, but a few donors experienced an urgent desire to defecate

**Hyperventilation and tetany** Various respiratory changes, such as slow, rapid, deep, shallow and intermittent breathing, were observed Of these, hyperventilation was the outstanding finding Following it the typical symptoms and signs of tetany were observed in 6 cases, with carpopedal spasm, a positive Chvostek sign and numbness, tingling and

investigators, however, and it is generally accepted that overbreathing in nervous persons with subsequent loss of carbon dioxide, causing a change in pH of the blood bathing the cerebral centers, is the most logical explanation of hyperventilation tetany <sup>6, 7</sup>

### CONSTITUTIONAL AND GENERAL FACTORS

**Age and sex** Young donors are much likelier to faint than are older ones Although 75 per cent of the cases of severe syncope occurred in donors between eighteen and thirty-eight years old, this age group comprised only 58 per cent of the total donors (Fig 1) There was little difference between the syncope rates in men and those in women On closer analysis, however, it becomes apparent that young women faint much oftener than any other group of donors As shown in Figure 2, 47 per cent of the women de-

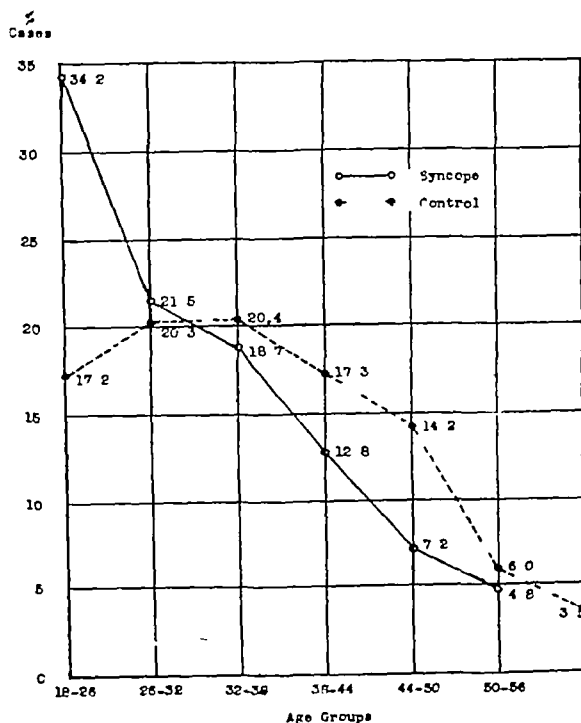


FIGURE 1 Relation of Age to Syncope

pain in the jaw and extremities One of these donors also presented evidence of syncope, although she did not lose consciousness

Tetany may occur without syncope, but tetany, convulsions and syncope may all occur in the same person Frazer and Forweather<sup>8</sup> recently described 7 cases of tetany in blood donors, in some of which there was a fall in blood inorganic phosphorus This finding has not been confirmed by other in-

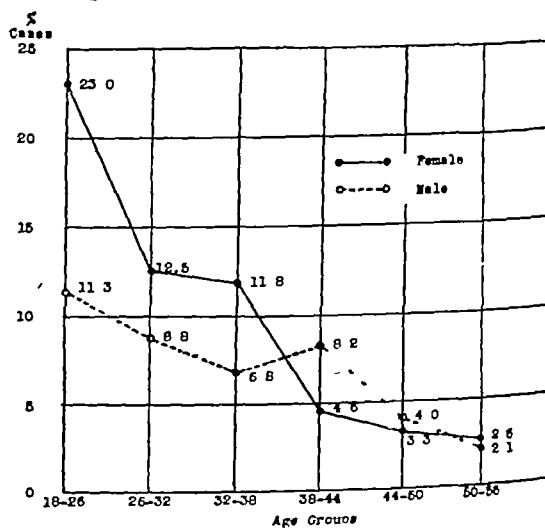


FIGURE 2 Relation of Age and Sex to Syncope

veloping severe syncope were between the ages of eighteen and thirty-eight, as compared with 29 per cent of the men

It is also interesting that in the few young women bled in the first series the syncope rate was 3 per cent, whereas in the second series, with many more young woman donors, it was 5 per cent

**Surface Area (Blood Volume) and Amount of Blood Withdrawn** It is generally believed that the amount of blood loss is an outstanding factor in the production of syncope in donors If this is true, there should be a relation between blood volume and syncope, provided that the amount of blood withdrawn is constant Poles and Boycott<sup>9</sup> found that the body surface of fainters was lower than that of non-fainters, but if it is accepted that approximately 1 square meter of body surface is equivalent to 3000 cc of blood, the difference in both sexes between syncope and control cases in the Poles and Boycott series amounted to an average of only 0.06 square meter or 180 cc of blood, a

## ELECTROENCEPHALOGRAPHIC STUDIES IN DIABETES MELLITUS\*

MILTON GREENBLATT, M D,† JEAN MURRAY, M D, AND HOWARD F ROOT, M D ‡

BOSTON

**E**LECTROENCEPHALOGRAPHIC studies have become an almost routine procedure at the New England Deaconess Hospital in examining diabetic patients who have frequent insulin reactions or seizures in which hypoglycemia is considered a possible precipitating factor. Although the incidence of epilepsy among diabetic patients has not proved to be greater than that in unselected persons of corresponding age groups, the occurrence of repeated insulin reactions in a specific case always raises the question whether they are due to an abnormally rapid change in the blood sugar or to instability of the nervous mechanism — that is, to an epileptoid tendency. The electroencephalogram was therefore invoked as an aid in studying the cortical activity of patients with diabetes mellitus to establish or rule out the existence of epilepsy.

It is known that diabetic patients are more sensitive to hypoglycemia than are persons with a normal carbohydrate metabolism — a fact that Root et al.<sup>1</sup> have recently demonstrated in their studies of radioactive insulin and its absorption. They examined normal controls and diabetic patients given identical doses — 25 units of crystalline insulin — and found that all the latter patients developed hypoglycemic reactions, as compared to only 1 of the controls.

In experiments on normal persons the brain waves are progressively slowed by a reduction of the blood-sugar level to below 50 to 60 mg per 100 cc, and this slowing is readily correlated with outward clinical manifestations.<sup>2,3</sup> The reduction of blood sugar in normal persons by means of insulin given for short periods of time produces no irreversible effects in the electroencephalogram. Injection of sugar restores the brain-wave frequency along a smooth curve.

It is not known whether repeated insulin reactions or hypoglycemic spells can eventually produce abnormal cerebral electrical activity. It will be shown, however, that in diabetic patients subject to repeated severe insulin reactions a startling degree of electroencephalographic abnormality exists. This may be due to inherent instability of the nervous system, to repeated deprivation of essential brain foodstuffs during hypoglycemia or to recurrent cerebral edema and minute petechial hemorrhages sustained during periods of profound hypoglycemia.

Himwich<sup>4</sup> has shown that profound hypoglycemia may depress the brain metabolism to one quarter of its normal rate. He mentions that a late and prolonged stage of hypoglycemia may produce permanent brain damage. Gellhorn and Kessler,<sup>5</sup> studying insulin-sensitive rats, found that insulin hypoglycemia produced the same type of effect on the electroencephalogram as that seen with anoxia.

Concerning nondiabetic epileptic patients, the evidence as presented by Gibbs et al.<sup>6</sup> is that a low blood-sugar level may increase the electrical abnormality in patients with petit mal, but does not do so in patients with grand mal or psychomotor epilepsy.

## TECHNIC

A Grass six-channel electroencephalogram with undistorted recording up to 50 cycles a second was used. Electrodes were applied to the frontal, parietal and occipital areas. Recordings were done in a darkened room with the patient's eyes closed. In all control subjects the blood-sugar level was determined shortly before the test. A two-minute period of overbreathing was included in every test. The records were classified as normal, borderline and abnormal, on the basis of experience with several thousand patients with and without neuropsychiatric disturbances.

## RESULTS

*Patients with Uncomplicated Diabetes*

A group of 40 patients with uncomplicated diabetes served as controls for 35 diabetic patients with repeated severe insulin reactions. The ages of the controls ranged from eighteen to forty-nine years with an average of thirty-four years. In this range one can expect the least number of variations in brain activity caused by immaturity or by senile changes. The previous duration of diabetes was one week to twenty-one years, and 20 patients had had the disease for ten years or more. The blood-sugar levels before the electroencephalographic examination ranged from 116 to 428 mg per 100 cc. All the patients were ambulatory and in good health. None of them had a history of seizures, personality change or neurologic disturbance. All patients but 1 were taking insulin, in doses ranging from 10 units of protamine-zinc insulin to 26 units of crystalline insulin and 76 units of protamine-zinc insulin.

The records were classified as within normal limits in 32 cases, as borderline in 5, and as distinctly abnormal in 3. Analysis of these three groups revealed no significant differences in age, sex, duration of diabetes, duration of insulin intake or type of in-

\*From the New England Deaconess Hospital and the Boston Psychopathic Hospital.

†Assistant in psychiatry Harvard Medical School senior physician and director of the Electroencephalographic Laboratory Boston Psychopathic Hospital.

‡Associate in medicine Harvard Medical School physician-in-chief New England Deaconess Hospital.

Lewis<sup>18</sup> and Weiss<sup>12, 14</sup> and to those observed more recently in blood donors by several British writers<sup>4, 8</sup>

It is evident that certain constitutional and contributory factors influence the production of syncope in blood donors. The young donors, especially women, were those most prone to fainting, and as suggested by Williams,<sup>10</sup> this may be due to an increased vasomotor instability in younger persons. It has been pointed out that in blood donors syncope differs from the usual form of fainting in that it frequently occurs with the donor in the supine position and usually develops following withdrawal of 500 cc of blood. Nevertheless, in this series syncope occurred without loss of blood and with the donor lying down, the attack simulating in every detail that occurring after withdrawal of blood. It seems obvious that although blood loss and posture may be important conditioning factors, they are not the *sine qua non* of syncope.

The physiologic mechanism of syncope is obscure, but its various and puzzling manifestations undoubtedly occur as a result of a number of reflex stimuli passing along both sympathetic and parasympathetic pathways. Recent studies by McMichael<sup>15</sup> indicate that in vasovagal collapse the fall in peripheral resistance is due to reflex dilatation of the arterioles in the skeletal muscles. It is evident that the work of McDowell<sup>2</sup> and other British investigators<sup>16</sup> will go far toward dispelling the obscurity surrounding the vasomotor and cardiovascular phenomena associated with syncope.

#### TREATMENT

Syncope may give rise to alarming symptoms, and in severe cases the patient may assume a death-like appearance. Indeed, in some cases it is impossible to detect a radial pulse or to obtain the blood pressure for several minutes. There is no doubt that such a severe vasomotor collapse could precipitate serious trouble in subjects with latent or potential organic cardiovascular disease. For this reason the elimination of those subject to fainting is an important consideration. In common with recent British opinion,<sup>17</sup> it is believed that donors with a history of prior fainting should be rejected as candidates for blood donation. The high incidence of a history of easy fainting—50 per cent of the cases of severe syncope in this investigation—has been noted by others.<sup>10, 17</sup> The use of donors who are excessively tired or nervous should also be avoided, and psychic factors should be eliminated in so far as possible.

For the immediate treatment of fainting the most effective measure is to place the patient in a supine position with the lower extremities elevated. It is

important to keep him at rest until the blood pressure has returned to normal levels to prevent re-collapse, which sometimes occurs after the donor has left the center, with subsequent fall and injury. The use of vasoconstrictor drugs such as N-methylamphetamine, as noted by McMichael,<sup>15</sup> may well be employed in severe cases of syncope.

#### SUMMARY AND CONCLUSIONS

In an experience with 16,133 blood donors, 689 cases of syncope were encountered, an incidence of 4.2 per cent.

Detailed observations on the symptoms and signs of severe syncope are recorded. Although these were often dramatic, in no case in this series were there any serious sequelae.

The frequent history of prior fainting in a series of cases of severe syncope is especially noteworthy, and the importance of psychogenic factors in syncope is emphasized.

Recent studies give promise of furnishing new insight into the complex physiologic mechanism involved in syncope, but there is much that remains obscure. The following statement of Gowers, quoted by Weiss,<sup>12</sup> seems as true today as it was in 1907: "Familiar as fainting is, adequately as we seem to know it, there is much in it that we do not know. Our knowledge is enough to obscure our ignorance."

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nificant fraction of cases present extreme difficulty in control by routine methods, and require special attention. These patients are inordinately sensitive to relatively minor changes in the blood-sugar level, and their clinical reactions are disproportionately severe. The manifestations of insulin sensitivity are highly variable.

In cases of this kind it is of both theoretical and practical importance to know what role the nervous mechanism plays in the fundamental instability. Because the changes primarily involve carbohydrates, the chief foodstuff of the brain, one is naturally inclined to suspect disordered function within the central nervous system. From the clinical point of view, many of the reactions involve abnormal but co-ordinated motor manifestations or specifically suggest epilepsy. Other reaction patterns such as unconsciousness, point incontrovertibly to abnormal cerebral function.

The electroencephalographic evidence supports the theory that severe repeated insulin reactions are due not only to unstable carbohydrate regulation but also to unstable cerebral, and specifically cortical, function as well. Some of the electroencephalograms obtained were indistinguishable from interval patterns in patients suffering from grand-mal epilepsy. The incidence of abnormal or atypical brain wave tracings in the unstable group of diabetic patients is too high to be due merely to chance.

The observations established the fact that the central nervous system plays a leading role in the instability of patients with so-called "problem diabetes" or diabetes regulated with great difficulty. In this group the possibility of cortical instability should never be neglected in evaluating the functional difficulties of the patient, and by implication, proper treatment should encompass proper management of the central-nervous-system disorder. The electroencephalogram may be invoked as a valuable aid in

studying diabetic patients with frequent severe insulin reactions.

### SUMMARY

In a study of 40 patients with uncomplicated diabetes, the incidence of cerebral dysrhythmia as evidenced by abnormal electroencephalograms is not increased over that in normal persons.

Long duration of diabetes does not alter the incidence of cerebral dysrhythmia.

Administration of insulin over long periods of time has no apparent effect on the electroencephalograms.

Fifty-one per cent of diabetic patients with frequent severe insulin reactions were found to have abnormal electroencephalograms.

The electroencephalograms are of aid in the evaluation of the stability of cortical function in diabetic patients with such reactions.

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sulin used The following is a brief summary of the controls with definitely abnormal electroencephalograms

**CASE 1 (No 22895)** A 47-year-old woman had been taking insulin since the onset of diabetes in 1929 The dosage at the time of the electroencephalographic study was 4 units of crystalline insulin and 26 units of protamine-zinc insulin On the maximum dose of 8 and 36 units, respectively, there were several mild reactions, with blood-sugar levels of 44 and 46 mg per 100 cc, but no convulsions or unconsciousness

**CASE 2 (No 13831)** A 47-year-old woman had had diabetes for 9 years Insulin had been given since 1935 At the time of the electroencephalogram she was receiving 28 units of crystalline insulin and 58 units of protamine-zinc insulin, which was the maximum dose She had a basal metabolic rate of +30 per cent, with toxic adenoma of the thyroid gland, which was later removed The electroencephalographic abnormality may have been related to the cerebral electrical disturbance of hyperthyroidism

**CASE 3 (No 7336)** A 43-year-old man, with diabetes of 15 years' duration, had taken insulin for the entire period, the dosage being 4 units of crystalline insulin and 20 units of protamine-zinc insulin The blood-sugar level at the time of the examination was 428 mg per 100 cc There had been a recent severe insulin reaction, with unconsciousness but no convulsions Insufficient insulin was taken by the patient because of fear of recurrence At a subsequent office visit he was ambulatory, with a blood-sugar level of 44 mg

These 3 patients comprise 8 per cent of the entire control group studied, which compares favorably with the incidence of cerebral dysrhythmia of 8 to 10 per cent in general unselected groups of non-diabetic persons Lennox<sup>7</sup> states, "It is important to realize that even though certain individuals, probably about 10 per cent of the population, have a cerebral dysrhythmia and, therefore, presumably carry a predisposition to seizure or allied conditions, such seizures or conditions may never eventuate unless one or more of the other causes of seizure are present"

In essentially uncomplicated diabetes of long duration, the figures for electroencephalographic abnormality are quite similar to those in uncomplicated diabetes of short duration Of the 20 patients with a long duration, — ten or more years, — 2 had abnormal electroencephalograms In 10 patients, the onset of diabetes had occurred before the age of fifteen years No one of these cases was recorded in the abnormal class, 2 were in the borderline group, and the other 8 were normal This may be of interest because of the increased incidence of epilepsy in diabetic children, in whom it is 1.07 per cent, as compared with 0.84 per cent in normal children<sup>8</sup> All classified as child diabetic patients have relatively severe diabetes and have taken insulin for a minimum of approximately fifteen years

#### *Diabetic Patients with Repeated Severe Insulin Reactions*

Thirty-five diabetic patients with repeated severe insulin reactions — problem cases — were also evaluated from the electroencephalographic point of view The clinical manifestations of these attacks included dizziness, weak spells, transient disturb-

ances of memory, aphasia or paresis, temper tantrums, attacks of petit mal, convulsive attacks and spells of unconsciousness In some cases hypoglycemia was known to be present and improvement occurred with the administration of carbohydrate All patients were studied between attacks, when they had no clinical symptoms of hypoglycemia

The ages varied from fourteen to fifty-four years with an average of 25.7 years The duration of diabetes ranged from 5 months to twenty years, with an average of 8.2 years Blood-sugar levels were not ascertained in all cases before the electroencephalographic tracings, but no patient had clinical symptoms of hypoglycemia at the time they were made All the patients were taking insulin in doses ranging from 8 crystalline and 16 protamine-zinc units to 36 crystalline and 78 protamine-zinc insulin units

The tracings were classified as normal in 8 cases, as borderline in 9, and as definitely abnormal in 18 There was no significant difference between these three groups in age, duration of diabetes, duration of insulin intake or type of insulin taken The types of insulin reaction in all groups were quite varied

#### DISCUSSION

Diabetic patients in general do not suffer from epileptic phenomena more than do members of a normal group Similarly, electroencephalograms in cases of uncomplicated diabetes are essentially

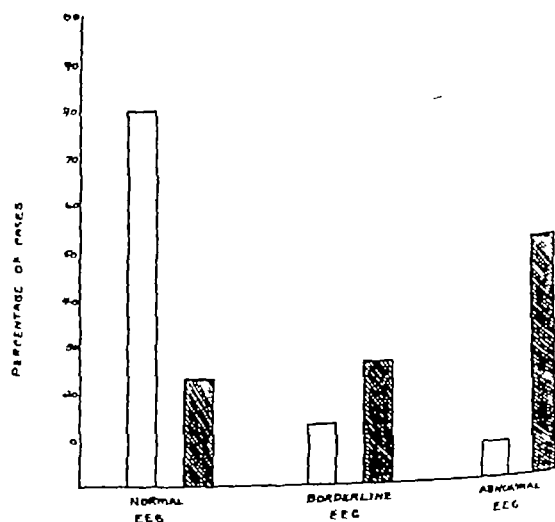


FIGURE 1 Percentage of Normal, Borderline and Abnormal Electroencephalograms in 40 Control Diabetic Patients and in 35 "Problem" Diabetic Patients

The blank blocks represent the control group, and the cross-hatched blocks the "problem" group

within normal limits This is true irrespective of the duration of diabetes, the duration of insulin treatment or the amount of insulin administered In clinics in which large groups of diabetic patients are studied, however, a small but nevertheless sig-

tween 1910 and 1915. There is now the pressure behind disability compensation. The original concept of workmen's compensation was one of weekly cash payments during the period of disability. This concept is held with respect to disability compensation. Soon after the initiation of workmen's compensation, the fact that people were not using their weekly payments to purchase necessary medical care became evident. It also became evident that the provision of medical care would "pay dividends." Hence, medical services were introduced as a part of workmen's compensation; the services have steadily increased, and today any proposal to exclude such services would be regarded as contrary to sound policy. The parallel presents itself in disability compensation. It will be interesting to see how long such a system as that in Rhode Island operates without medical services as a part of the scheme.

There are many questions that involve the combination of independent group practice and group payment. Here, too, the administrator thinks in terms of practical application. The qualitative values of group practice are seldom questioned, but within the group, recognition must be given to certain essentials: the income for each member must be reasonably adequate, and his tenure as a member of the group must be reasonably stable. Assuming that a group is organized to serve 50,000 people on a voluntary prepayment basis, the population must be one whose income is stable. Thus, it cannot be one of 50,000 today and one of 30,000 a year later owing to unemployment. A medical group dependent for its stability on a continuing income and having a staff large enough to care for 50,000 people might weather a short-term decrease to 30,000, but it could not weather a long-term one. It is for this reason that the most successful medical group practice under a system of voluntary prepayment is the one that includes that small portion of the population with stable incomes — policemen, firemen, schoolteachers and others with annual salaries. To include industrial populations with extremely fluctuating levels of employment means that the medical group must face the difficult problem of preparing against abrupt decreases in income. If this preparation is inadequate or impossible and the emergency comes, the group is threatened with disintegration.

Mention has been made of voluntary prepayment. The question of compulsion *versus* volition is presented as one of the sharpest issues of the day. But it is not really so sharp as it has been drawn. There are many forms of compulsion other than legal. There is the pressure of sales, the pressure of group or public opinion, the moral pressure of employers on employees and the even greater pressure exerted by employer contributions as partial payment. Actually, the issue is becoming less and less one of compulsion *versus* volition and more and more one of legal compulsion *versus* quasi-compulsion.

There is another broad generalization that calls for much more critical examination. It has to do with the method of compensation for services, from the administrative standpoint it causes apprehension. The evidence is fairly clear that, whatever the future prepayment plan for medical care, it will begin with fees for specified services as the method of compensation to physicians. There may be changes to so-called "capitation fees" or ultimately to salaried services, but the administrator must deal with immediate problems, not with ultimate possibilities.

The fee-for-service method of payment has a long and broad history of failure. It is unlikely that it will work merely because of resolutions that describe it in flattering terms and declare it to be "the American way." Not only did it fail yesterday but it is failing today. Even though an appendectomy rate of 25 per 1000 subscribers, for example, does not endanger the economic foundation of a prepayment plan, such a rate is approximately triple the normal one and points to a need for administrative action; absence of action means another failure for the system. "Control" is a hated word, but the application of necessary and fair control measures is not nearly so dangerous as is the continued evasion of brutal facts. The fee-for-service method if applied with all the ingenuity of which administrations are capable might be made to work, applied without such ingenuity it has in it the elements of a national calamity.

The final example of administrative problems in prepayment programs relates to the two major forms of the benefits to subscribers. In one case the subscriber's contract calls for services, in the other, the benefits are distributed in cash. In the first case, the subscriber would receive an appendectomy and the surgeon would be compensated directly from the fund, probably receiving \$100 as full payment for the service. In the second case, when the subscriber presents written evidence that an appendectomy has been performed, the company or the plan indemnifies him, a check being sent either to him or directly to the surgeon.

All this appears to be six of one and half a dozen of the other. Whereas the great majority of the voluntary plans provide services, the insurance company plans indemnify in cash. It is the recommendation of many medical societies that the principle of cash indemnity be applied, yet if the principle is widely applied, it is doubtful that it can withstand the accumulative weight of public disfavor.

As an insurance device, cash indemnity as now used is unsound. The subscriber purchases in good faith what he interprets as protection, but not until the contingency arises is he able to learn the degree of his protection. It may be 100 per cent or 50 per cent, depending on the charge for the service. No other form of insurance could exist if this principle

## SYMPOSIUM ON MEDICAL SOCIOLOGY

## MEDICAL ECONOMICS\*

NATHAN SINAI, D P H †

THE title of this lecture is actually the inclusive title of the entire series. The series can serve only to provide a superficial view of the issues involved. If out of this view there emerges a continuing and critical analysis, the series will have had high value. If, on the other hand, the series ends with final decisions on the part of the audience, it must be concluded either that these decisions were brought to the meetings or that the speakers were highly persuasive.

In arriving at conclusions, there is an acute need throughout the country for the tested device that is such a common procedure in medicine—the device embraced in the words “examination, diagnosis, treatment.” The fallacy of centering attention on treatment without any agreement concerning diagnosis, which, in turn, is based on a critical examination, is obvious. It is so obvious that one wonders at its prevalence. Because of this prevalence, about two thirds of the courses in this field for sophomore and senior medical students at the University of Michigan are purposely devoted to “examination and diagnosis.”

There is one aspect of medical economics to which attention has been pitifully inadequate. Most of the discussions in the country have revolved around broad principles, broad philosophies, broad plans and broad legislation. Their very breadth excites passionate debate, but ultimately, whatever principles, philosophies, plans or legislation are adopted, these must be transformed into the realities and details of administration. So far, this fact has almost entirely escaped attention. Because of this, and in spite of the discussion, the average physician is unable to see himself and his concept of practice within the framework of any scheme that may be proposed. What are needed are fewer panoramas and many more “closeups.” Some of the problems and situations that administrators must face within the framework of various broad proposals are the following:

The statement is generally accepted that the public wants and needs medical protection against so-called “catastrophic illness,” but there is a tendency to leap from this to the conclusion that practically all medicoeconomic catastrophes involve the

hospital and either the surgeon or the obstetrician. It is said that 10 per cent of the people pay 41 per cent of the total medical bill, the hospital, the surgeon and the obstetrician being the chief payees. But a few other facts and diagrams insist on obtruding themselves, and the word “catastrophe” then becomes less easy to define in terms of absolute costs. Indeed, it becomes a relative matter closely linked to the income groups in the country.

It will be recalled that the Wagner-Murray-Dingell Bill proposes to exclude the services of dentists. The decision to exclude them was probably based on the knowledge of the overwhelming number of existing dental defects and the lack of enough dentists to cope with the problem as a whole. Practically all those who questioned the exclusion thought in terms of at least a partial attack on the problems, especially with respect to the needs of children, but from the administrative standpoint, the exclusion raised an entirely different question.

In many parts of the country a large portion of the oral surgery is performed by specialists whose training and professional degrees are in dentistry. They are the ones who provide services in such cases as jaw fractures. If the exclusion of dentists had been adopted, the bill would have created an anomalous situation in which the services would have been included, but the many specialists who provide them would have been excluded. It is not intended to imply that this was the intention of the authors of the bill, the statement is only one of what would have happened in its administration.

To the administrator, the role of medical care as a buttress for other systems of security is a weighty one. It is estimated that by the end of the next thirty years persons above the age of sixty will comprise almost a fifth of the population. Only a cursory examination of the curve of illness according to age is necessary to reach the conclusion that old-age annuities cannot provide protection against the concentration of illness in the upper age groups. The same general conclusion is warranted as concerns unemployment payments under a system of unemployment insurance.

On the subject of security, another movement taking place in the country deserves much more attention. It is the movement toward disability compensation. There is danger in reasoning by exact analogy, but the only greater danger lies in discarding all previous experience. Workmen's compensation legislation swept the country be-

\*This is the fourth of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March, 1945. They were sponsored by the Department of Preventive Medicine and were primarily intended for third year students. These articles will temporarily replace the reports “Medical Progress.”

†Professor of public health, University of Michigan, Ann Arbor, Michigan.

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32041

#### PRESENTATION OF CASE

A twenty-nine-year-old clerk entered the hospital complaining of recurrent pain in the flanks.

Eight years before admission he had an attack of sharp pain in the right flank, and later passed several stones by urethra, followed by slight bleeding, which lasted for thirty hours. Another stone was passed two years later, and on chemical analysis was found to consist of calcium phosphate. A third attack of pain in the right flank and passage of stones occurred three years before admission, while in the Army. Similar episodes recurred four and eight months later. The sixth passage of stones took place eight months before admission, at that time another stone was detected by x-ray examination in the right renal pelvis and a right nephrolithotomy was performed. Several weeks later, pain was noticed in the left flank for the first time and stones were again passed. The patient was later discharged from the Army.

Weakness and fatigue had not been marked. For three years, however, the patient had not been able to resume the upright position after leaning over. No polyuria, frequency or evidence of renal infection had been noted. The appetite had been good, and he had complained of no bone pain. Four years before admission he had sustained a traumatic fracture of the left fifth metacarpal, healing was normal. The teeth had been in good condition. His maximum weight had been 140 pounds, three years before admission, at the time of admission his weight was 120 pounds, with no recent loss.

Physical examination revealed a thin, pale man in no discomfort. The pharynx was moderately injected, with a postnasal drip. The teeth were normal. The trachea was slightly deviated to the left, with a questionable soft-tissue fullness on the left. The heart was not enlarged. A soft systolic murmur was heard over the apex. The lungs were clear. There was no costovertebral-angle tenderness. The bones were normal. Neurologic examination was negative.

The temperature was 99.2°F, the pulse 80, and the respirations 20. The blood pressure was 130 systolic, 75 diastolic.

The hemoglobin was 14.7 gm. The urine contained an occasional white cell, mucin and calcium oxalate crystals. A twenty-four-hour urine specimen, which had a volume of 1688 cc., contained a total of 288 mg of calcium. The serum calcium was 10.7 mg per 100 cc, the phosphorus 3.0 mg, and the alkaline phosphatase 4.0 Bodansky units. Determinations the next day were as follows: serum calcium 10.7 mg per 100 cc., phosphorus 3.1 mg, and alkaline phosphatase 4.9 units. The total serum protein was 6.0 gm per 100 cc. A blood Hinton test was negative.

An x-ray film of the teeth showed no parodontal disease, the lamina dura was preserved but of unusual thickness. The bones of the jaw were not so dense as usual, and the trabeculae were coarse. The bones of the lumbar spine and pelvis, the upper portions of the femurs and the lower ribs showed some decalcification, the cortices were thinned, and the trabeculae coarse. No urinary calculi were evident. Several areas of increased density overlay the cecum.

An operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. ALLAN M. BUTLER: Either the clinicians who took care of this patient were extremely wise or they had more data than those given in this abstract on which to base the decision to perform an operation. We have no information about renal function. We have only the statement that no evidence of renal infection was found on one examination. There was no intravenous pyelogram, and no determination of the serum carbon dioxide and chloride. Is that correct?

DR. BENJAMIN CASTLEMAN: We have given you all the information that was in the record.

DR. BUTLER: Then I must confess that, not being so intelligent as the physicians who took care of this patient, I should have demanded that information before doing an operation.

We shall now consider the x-ray films. I wish that we had a roentgenologist to interpret them, for I see nothing suggesting why this man was unable to resume the upright position after leaning over. Do you see anything in the films, Dr. Aub, that would cause this?

DR. JOSEPH C. AUB: No.

DR. BUTLER: Of course, one thinks of arthritis and of intervertebral disk, but without a roentgenologist, I shall pass on.

DR. AUB: I think there is a little decalcification.

DR. BUTLER: Yes, but it appears minor.

DR. AUB: I am not so sure.

DR. CASTLEMAN: The x-ray report states that there was some decalcification. The cortices were thin.

were used — if the protection purchased remained a mystery to the purchaser until he needed protection

From the public viewpoint, and considered in terms of reality certain responses to the situation in some existing plans are disturbing. When a patient who carries hospital-service insurance but has cash-indemnity medical protection inquires what a surgical fee will be, he may be asked whether he carries hospital insurance and surgical insurance, and if he replies in the affirmative the surgeon may say "That's very fortunate. It is a fine thing to have such protection. My fee will be \$200." The question about insurance may not be so abrupt or so pointed, but however it is put, the patient is aware that he has answered it. Too often a by-product of the experience, whether or not it is justified, is an unanswered question in the mind of the patient and concerning whether the fee was much larger as a result of the protection than it would have been without such protection. This question does not leave the physician in an enviable position.

Its end result, a loss of public confidence, is predictable in terms of public antagonism.

Enough has been said to indicate a primary need for practical methods in medical economics. Without far more attention to administrative methods and details and to the organization of administrative experience, no plan can proceed from broad principles to satisfactory applications. It is administrative method that will influence and finally determine the medical, social and economic soundness of any plan.

Over the country there is abundant administrative experience, but it is a misfortune that so little of it has been accumulated. Except for experience with hospitalization plans in connection with Blue Cross organizations, there has been little centralization of experience. It is for this reason that in our own work at the University of Michigan we have emphasized administration and administrative technics.

This man had been in the armed forces and at time of discharge was referred to this hospital. We tried to get the medical history from the Army. He reported that he had been sent in with a question of hyperparathyroidism because the blood chemical findings while he was in the Army had been quite abnormal. (The phosphorus values were reported to be between 2.9 and 4 mg and the calcium as high as 14 mg per 100 cc.) The medical officer considered a diagnosis of hyperparathyroidism and suggested to the patient on discharge that he come here for further study. Our records include some additional data. The patient had a negative urinary culture, and although we examined the urinary sediment quite carefully we could find no evidence of urinary infection. We too ruled out a renal condition as a cause for the abnormal blood chemical findings.

DR ALBRIGHT: Why did Dr. Butler think of parathyroid hypertrophy?

DR BUTLER: Because of your work, Dr. Albright.

DR ALBRIGHT: The disease is extremely rare.

DR BUTLER: You reported an excellent series of cases in the *Archives of Internal Medicine*?

DR OLIVER COPE: I might say that the patient was here during the peak of the shortage of x-ray films, which explains some of the lack of films. The X-Ray Department only had a day or two's supply of film on hand and asked us to cut down on any unnecessary examinations. We were a little confused because the original serum calcium determinations in the Army were 14 and 12 mg, and it looked as if these values were accurate. Our values were lower than anticipated. Three determinations were below 11 mg per 100 cc, and we have accepted this as the minimum to make a diagnosis of hyperparathyroidism. That discrepancy, of course, contributed to the confusion and is emphasized because so much stress has been placed on the level of the serum calcium.

We thought that this patient had hyperparathyroidism, and I explored the right side of the neck first on a 50-50 chance. I could not find an enlarged parathyroid gland on the right side, so I went to the left and after exposing the posterolateral surface of the thyroid gland, I saw some vessels that should not have been there. They were a little large, and they went down behind the thyroid gland and the esophagus. I found what appeared to be a small adenoma in the upper gland. It was round and light in color—in parathyroid hypertrophy the glands are irregular in shape and a little more chocolate in color than an adenoma. I then found quite easily a lower parathyroid gland on the left, which appeared to be normal in size and to have the correct color.

#### CLINICAL DIAGNOSIS

Parathyroid adenoma

#### DR BUTLER'S DIAGNOSIS

Hyperparathyroidism due to either a small adenoma or idiopathic hypertrophy

#### ANATOMICAL DIAGNOSIS

Parathyroid adenoma

#### PATHOLOGICAL DISCUSSION

DR CASTLEMAN: This was a small adenoma, measuring about 8 by 6 by 4 mm. A normal gland measures 6 by 4 by 2 mm. There was a rim of normal parathyroid tissue around a part of the adenoma, which is what one should always look for in making a section of an adenoma. The presence of this rim of normal gland is evidence in favor of neoplasm and rules out hyperplasia. Hyperplasia involves the entire gland and does not leave a rim of perfectly normal tissue.

DR REIFENSTEIN: The blood chemical findings after operation are of interest. On the following day the calcium was 8.7 mg, and the phosphorus 2.6 mg per 100 cc. Three days after operation the phosphorus was 3.8 mg and the alkaline phosphatase 3.0 Bodansky units, and on the fourth day the calcium was 8.0 mg, the phosphorus 3.7 mg, and the phosphatase 1.9 units. The Sulkowitch test for calcium in the urine was +++ before operation, +++ two days after operation, and + to zero thereafter.

DR CASTLEMAN: Do you think that we should consider a serum calcium of 10.7 mg as being above normal?

DR BUTLER: The upper limit of normal, with a normal serum protein, is about 10.5 mg. This patient's serum protein, however, was down to 6 gm per cent.

DR ALBRIGHT: Our average normal runs about 9.5 mg per 100 cc.

DR BUTLER: The serum protein concentration of most hospitalized patients is down a little, and that means the serum calcium concentration is correspondingly lowered.

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#### CASE 32042

#### PRESENTATION OF CASE

A seventeen-year-old schoolgirl entered the hospital complaining of pain in the right pubic region.

Six months before admission she first noticed a "nagging" pain in this area. It grew steadily severer and came to involve the right hip and thigh down to the knee. She walked with a limp and with increasing difficulty. She had lost about 10 pounds

DR BUTLER The trachea was slightly deviated to the left, with a question of fullness on the left. We have no x-ray films of the neck region. Parathyroid tumors are almost never palpable. The deviation was to the left and the fullness was on the left. I shall pass that over, because I cannot explain it.

At the end it states that several areas of increased density overlay the cecum. I am unable to interpret the significance of these spots, and I take it that the x-ray man could not interpret them.

We then come to a discussion of the etiology of the renal calculi, from which this man had suffered for eight years. First, we think of renal disease. It may be infection, particularly with an ammonia-producing organism. We merely have this single statement in the record that there was no evidence of renal infection. So our evidence regarding infection is extremely meager.

DR FULLER ALBRIGHT There were two negative cultures.

DR BUTLER That being the case, at the time of his last examination he did not have evidence of renal infection, but that, of course, does not rule it out.

The next thing to consider is renal stasis. The evidence again is meager, because we have no information about a renal-function test and an intravenous pyelogram. There is a type of renal disease associated with diminished ability of the kidneys to produce ammonia and thus to conserve base in the excretion of urine; this results in excessive loss of calcium and other cations (base) and thus in acidosis.

DR ALBRIGHT The serum carbon dioxide and chloride levels were normal.

DR BUTLER Serum chloride in patients with renal calculi is not infrequently found to be elevated, and because of that elevation, there is a diminished carbon dioxide, and a chloride acidosis, which accentuates the acidosis that comes from the loss of base just referred to above. This type of renal disease, with the chloride acidosis, loss of base and increased excretion of calcium, is usually a disease limited to the renal tubules, and in the tubules there is not infrequently a deposition of calcium phosphate. All the evidence so far is against that type of renal disease, largely because if there is an acidosis with any type of renal disease, and an excessive loss of calcium in the urine, the patient usually has an elevated alkaline phosphatase of the serum. Here the alkaline phosphatase of the serum was normal.

Then we come to cases of extensive renal disease, with renal insufficiency. This can be ruled out promptly with the data available, because with that type there should be an elevated nonprotein nitrogen and inorganic phosphorus, a diminished serum calcium and carbon dioxide and an elevated phosphatase, none of which were present in this case.

The second major cause of renal calculi that one

ought to think of is atrophy of bone. One might think of atrophy of disuse. In this case, however, the history is not indicative of atrophy associated with disuse. Dr Albright has recently called attention to a patient who presented a difficult differential diagnosis between hyperparathyroidism and atrophy of disuse. Dr Howard,<sup>1</sup> of Baltimore, has called attention to a patient who, following a fracture, was given a large amount of vitamin D and developed hypercalcemia, anuria and uremia. We have had a fairly extensive series of cases of so-called "resistant" rickets and have found that, following corrective osteotomies, there is often a marked elevation in the serum calcium and in organic phosphorus, a fall in the alkaline phosphatase to normal and complete healing of the rickets, which for years had been resistant to treatment with huge daily doses of vitamin D.

Another cause of bone atrophy may be Cushing's syndrome. There is, however, no history suggestive of a Cushing syndrome. Of course, if the demineralization of the bones as shown by x-ray were due to steatorrhea, there would not be increased calcium in the urine and calculi.

Finally, we come to hyperparathyroidism. Dr Albright and his colleagues have described a disease that can occur with minimal bone disease, but in most of the cases that they have reported there has been some elevation of the serum calcium. Because of the long-standing condition in this patient, however, and the demineralization and depletion of calcium, hyperparathyroidism may have been present without elevation of the serum calcium. Their cases showed a minimal change in the inorganic phosphorus and no elevation of the phosphatase. This patient's inorganic phosphorus was just at the lower limit of normal. The calcium of 10.7 mg for a serum protein of 6 gm is just above the upper limit of normal, by the accurate method used here.

In the absence of evidence pointing to renal infection and in the absence of such lowered carbon dioxide and of elevated phosphatase as would be consistent with a renal condition that would result in this much decalcification of bone and this degree of increased excretion of calcium, my diagnosis is either a small parathyroid adenoma or a so-called "idiopathic hypertrophy" of the parathyroid glands.

DR CASTLEMAN Hypertrophy of all four glands?

DR BUTLER The idiopathic hypertrophy that involves all four glands, the enlargement being due to an enlargement of the cells rather than to a great increase in the number of cells, such as one sees in secondary parathyroid hyperplasia following renal disease.

DR CASTLEMAN Dr Reifenshtein, would you like to comment?

DR EDWARD C REIFENSTEIN There is not much that I can add to the discussion, except to say that we never did obtain an adequate medical history.

not seen without other manifestations of the disease. In addition, this disease usually arises in the neighborhood of the joint and involves the capsule and cartilage.

Syphilis can be eliminated on the basis of the site, the character of the lesion, the age of the patient and, particularly, the absence of other evidence.

Other lesions in which the etiology is less definite must also be considered. Eosinophilic granuloma is frequently seen in young people, may occur anywhere, but generally in flat bones, and may give symptoms of pain and evidence of tumor. X-ray examination usually reveals a destructive lesion. It is seldom debilitating, however, and rarely gives rise to such symptoms as described in this patient. Osteoid osteoma usually presents as a small lesion and causes few symptoms. On x-ray examination it stands out from the surrounding osseous tissue as a delimited nidus, and there is evidence of calcified atypical new bone.

What are the possibilities of neoplastic disease? The history, symptoms and physical findings strongly suggest a neoplastic process. Osteochondroma, a benign lesion, may appear in the pubis but it can be eliminated by the x-ray evidence itself. Of the malignant lesions, there are a number of possibilities. Malignant lymphoma involving bone, particularly the reticulum-cell sarcoma type, may primarily arise in a single bone and remain confined in that location for a considerable time. It usually, however, is slowly growing and is rare in the pubis, and there are seldom constitutional symptoms, even when the tumor becomes large. Although it may exhibit evidence of bone destruction by x-ray, a soft-tissue mass is rare, except in certain locations.

Osteogenic sarcoma generally arises in the metaphyses of long bones, although one type especially, the chondrosarcoma, may arise in the pubis. Even the latter is unusual in this location. These tumors are usually prevented by the periosteum from breaking through and invading the soft tissue for a considerable period. When the soft tissues are invaded there may be evidence of calcification. In this patient there was no elevation of the alkaline phosphatase, but this does not eliminate an osteogenic tumor, particularly one of the osteolytic type. The x-ray films are not characteristic of an osteogenic sarcoma, although there is periosteal reaction, which in itself is insufficient to make a diagnosis. Pain is frequently an early symptom, but except in the late stages of the disease, disability is usually absent and the general status of the patient is surprisingly good and out of proportion to the extent of disease and the degree of malignancy.

Meloma usually occurs in persons over forty and is generally present in multiple sites when the patient is first seen.

Metastatic lesions from primary tumors elsewhere

are unusual in this age group and seldom give rise to soft-tissue tumors.

The one tumor that fits the clinical syndrome is Ewing's sarcoma. It is a tumor of growing bone and arises from the bone marrow. The long bones are usually affected, but flat bones, particularly those of the pelvis, are not infrequently involved. The disease causes bone destruction as it develops, and by x-ray the bone has a moth-eaten look. The periosteum becomes reactive and lays down new bone, often in layers, leading to the characteristic onion-skin appearance. Sometimes radiating spicules may be seen, thus causing confusion with osteogenic sarcoma. The disease may penetrate the periosteum. This is especially true in flat bones, where the tumor breaks through the periosteum early and invades the soft tissue, such as occurred in this case. There is seldom evidence of new-bone formation in the soft-tissue mass. Pain is the most frequent initial symptom. At first it is intermittent, but as the disease proceeds it becomes increasingly severe and persistent. The tumor usually cannot be palpated until a considerable time after the onset of symptoms. It is frequently tender, firm and irregular. The overlying skin may be warm, red and edematous, which not infrequently leads to an erroneous diagnosis of osteomyelitis. Although there is no such statement in the history, the disease is often accompanied by bouts of febrile reactions, which also suggest an inflammatory process. Constitutional changes, such as weakness and loss of weight, are often seen in Ewing's sarcoma. Pain and sensory disturbances arise from growth of the tumor within the marrow cavity and eventual involvement of the sensory nerves. Depending on the location, difficulty in motion and a lump may result from soft-tissue as well as motor-nerve involvement. Laboratory evidence is of little aid in the diagnosis. Occasionally the white-cell count is abnormal, but the alkaline phosphatase is rarely elevated.

In view of the above facts the most probable diagnosis is Ewing's sarcoma.

DR SCHULZ: It might be noted that within the past two years, we have seen at least three patients with Ewing's tumor in a comparable location.

DR ERNEST M. DALAND: This patient was operated on under novocain anesthesia. A palpable lymph node overlying the ascending ramus was removed, it appeared to be merely hyperplastic. The incision was deepened down to the bone, and tumor was found. A specimen was removed with a curet. There was a gush of white fluid that at first suggested pus but then seemed more typical of the fluid often seen with Ewing's sarcoma. The wound was closed without drainage.

#### CLINICAL DIAGNOSIS

Ewing's sarcoma of pubis?



in weight during her illness and had become definitely weak and anorexic

The past history was negative except that one year before admission the patient had bruised her right hip in an accident. Two years before admission, she had had an attack of "arthritis" in the knees.

Physical examination revealed a somewhat undernourished, sallow girl in no acute distress. Examination of the head, neck, heart, lungs and abdomen was negative. Attached to the right pubic ramus

## DIFFERENTIAL DIAGNOSIS

DR IRA T NATHANSON May we see the x ray films?

DR MILFORD D SCHULZ These films show an area of destruction involving the right pubic bone. A soft-tissue mass can be seen about it, into which spicules of bone extend. There is so-called "layering" where the periosteum has been lifted, and there seems to be a lot of disorganization of the normal medullary pattern. No remote disease is evident.



FIGURE 1 *Roentgenogram of Pelvis*

near the midline was a tender hard mass. There was tenderness also over the anterior aspect of the right femur and knee.

The temperature was 99°F, the pulse 100, and the respirations 25. The blood pressure was 120 systolic, 80 diastolic.

The hemoglobin was 12.2 gm. The white-cell count was 10,400, with 59 per cent neutrophils. The red cells and platelets appeared normal in a stained smear. The serum calcium was 9.6 mg per 100 cc, the phosphorus 2.4 mg, and the alkaline phosphatase 3.2 Bodansky units. The urine was normal.

An x-ray film of the pelvis revealed a destructive lesion involving the right superior ramus of the pubis and extending from the symphysis well toward the acetabulum (Fig 1). There was some periosteal reaction about it, and apparently a soft-tissue tumor into which radiating spicules extended. No other bony lesions were found. The lungs were clear.

An operation was performed.

DR NATHANSON An essential point to be considered in the diagnosis is whether the lesion is inflammatory or neoplastic. I shall discuss inflammatory lesions first.

Osteomyelitis is one of the most frequent of the inflammatory lesions. In favor of this diagnosis are the age of the patient, the pain and the progressive character of the process. Against it are the x-ray evidence of destruction of the periosteum, as suggested by a soft-tissue tumor, and the lack of the sequestration and new-bone formation usually seen in an osteomyelitis of relatively long duration. In osteomyelitis the periosteum is elevated but seldom penetrated. The site of the lesion is also unusual for such a disease. The white-cell count may be elevated but not necessarily so, particularly in the chronic phase of the disease. Loss of weight and generalized debility are uncommon except in the late stages.

Tuberculosis is extremely rare in the pubis, and as a rule, tuberculous lesions of this character are

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## FEDERAL SUPPORT FOR SCIENCE IN PEACETIME

PENICILLIN and the atomic bomb, with their enormous but opposite potentialities for good and for evil, were brought into a world at war by scientists subsidized by the federal government. These and other achievements of integrated scientific endeavor financed by federal grants have suggested the extent of the benefits that might accrue to our society in peacetime as a result of governmentally subsidized research. Over a year ago the late President Roosevelt sought an opinion on this matter from Dr. Vannevar Bush, director of the Office of Scientific Research and Development. The reply given by Dr. Bush<sup>1</sup> was written after consultation with committees of experts on medical science, natural science, the discovery of scientific talent and

the publication of scientific information. The report leaves no doubt in the mind of the reader concerning the immense potential advantages of a vigorous and flourishing science for improving human knowledge, economic status and health.

The need for federal support of scientific research arises primarily from the fact that the latter is expensive. Research, especially so-called "basic research," is a necessary preliminary to the applications of science, which are so obviously useful to medicine and other subjects. Basic research is carried out for the most part in universities or in nonprofit research institutes. It is often time consuming, always obscure and, because it seldom leads directly to practical results, seems to yield little tangible value relative to its cost. Applied research also is often expensive, but with practical objectives already clearly in view it is likelier to receive support from industry or other private sources than is basic science. Unfortunately, there is ample evidence that research is receiving progressively less support in the form of income from endowment, grants from foundations and private donations. Indeed, many of the seventy-seven medical schools in this country have never had sufficient funds to carry on more than a small amount of investigation. There is also a chronic deficiency of trained scientific talent, and this scarcity has been acutely increased by diversion to the battle fronts of students who otherwise would be preparing for careers in science. To restore university research even to its prewar level of scientific personnel will be a costly and prolonged educational undertaking. To accelerate scientific progress by discovering and fully utilizing the scientific talent and by developing the necessary laboratories of the country as a whole exceeds the capacity of the private sources of income that can be visualized today.

As physicians, we are impressed in our daily lives with the difficulties of appropriately applying the established findings of medical science to the individual patient. Yet, it is only necessary to consider the increasing incidence of cancer and degenerative diseases and of mental illness to understand that more hospitals and better diagnostic procedures, however useful, do not provide a solution. Better educational facilities for doctors also

## DR NATHANSON'S DIAGNOSIS

Ewing's sarcoma of pubis

## ANATOMICAL DIAGNOSIS

**Ewing's sarcoma of pubis.**

## PATHOLOGICAL DISCUSSION

DR BENJAMIN CASTLEMAN The biopsy confirmed Dr Nathanson's diagnosis of Ewing's sarcoma. The lymph node showed only hyperplasia.

DR DALAND The patient was treated with the million-volt machine, receiving a total of 5400r, half anteriorly and half posteriorly, over a period of approximately three weeks. After the second treatment she had practically complete relief. After the fourth treatment she was able to move her leg quite normally and opiates were stopped. By the time the treatments were completed, she had complete relief of pain and normal hip motion.

d would tend to promote the special interests of these governmental departments. They contend that, although knowledge of and liaison with governmental scientific activities should be maintained, the board should not be burdened with "efficiently organizing and co-ordinating all federally financed research and development," as recommended by the Kilgore Bill. On the subject of the management of patients arising in the course of research supported in whole or in part by the foundation, the Magnuson Bill is silent. The members of the Committee Supporting the Bush Report regard this mission as desirable, because they believe that to specify a partial solution of this complex problem, as is attempted in the Kilgore Bill, is premature in view of the fact that a study of the Government's patent policy is now in progress by a committee headed by the Secretary of Commerce.

In his message to Congress President Truman recommended the inclusion of the social sciences within the framework of the proposed foundation. Both bills as presented to the Senate committees in amended form include the social sciences — sociology, political science, economics, law and so forth — as fields in which scientific research and development are to be supported. Although recognizing the national importance of social studies, the Committee Supporting the Bush Report expresses the view that a board fully competent to administer grants for research and fellowships in the basic sciences would not be qualified for corresponding duties with respect to the social sciences. Consequently, it is suggested that the subject of research and education in the social sciences should be taken care of in a separate body, set up, presumably, after a factual study of the needs for federal support of the social sciences comparable to that which led to the framing of the Bush report.

On December 21, a third bill, sponsored by Senators Kilgore, Johnson, Pepper, Fulbright and Saltonstall was introduced. This bill retains the general objectives with respect to research and education of its predecessors, and meets some of the objections to the Kilgore Bill that have been raised by the Committee Supporting the Bush Report. Thus, *ex-officio* representation of governmental

departments is not required on the advisory board, but is provided for in a separate interdepartmental committee. The administrator, who is appointed by the President remains in charge of the foundation. He is required to consult and advise with a board composed of nine persons appointed by the President but also including the chairmen of from eight to eleven divisional scientific committees appointed by himself with the approval of the board. Patents taken out in the course of research and development authorized by contracts between the foundation or any other governmental agency and a private organization are, with certain exceptions, based on the extent of the latter's contribution, to be freely dedicated to the public. A division of social sciences is retained. Expenditure of 25 per cent of the funds is placed beyond the judgment and discretion of the administrator and his committees. It is provided that this sum be distributed among the tax-supported colleges and universities, including the land-grant colleges, according to a formula based partly on state populations. The germ of this proposal appears nowhere in the Bush report.

Subsequently, another group of scientists, comprising the Committee for a National Science Foundation, released a statement outlining its views concerning the feasibility and practicability of scientific advance under governmental auspices. The six major points are as follows: the necessity for federal support of research to supplement private funds, the inclusion of provision for all fields of fundamental scientific inquiry relative to national interest, the publication of findings resulting from federally financed research and dedication of these findings to "the welfare of the people", the training of research personnel, and the devising of a plan of organization that meets the major objections to vesting administrative responsibility in either a governing board or a single administrator.

Obviously there can be honest differences of opinion concerning the best legislative approach to the vital problem of federal support for the scientific endeavor of the Nation. In accordance with democratic procedure, the evidence for these different points of view has been presented at the Senate hearings, and it is to be hoped that Congress

will not suffice, for nowhere in the world today exists the knowledge of how to prevent or cure many of the important causes of death or chronic disability. If medicine is to continue to advance, science has to find the answers

Granted then that the need for research is so great that federal support is required, the question of fundamental importance to scientists and the public is whether such powerful assistance can be given without impairing the independence, imagination and freedom in experimental endeavor of the individual investigator, which is so essential for scientific progress. The Bush report considers that this is possible, provided that certain basic principles remain inviolate. Thus, there must be stability of funds for long-range programs administered by an agency headed by competent and impartial citizens.

The agency should promote research in organizations outside the federal government, and to these should be left, so far as possible, the choice of subject and method of investigation.

Last July the essential purposes and plan of the organization outlined by the Bush report were embodied in a bill that was introduced by Senator Magnuson, of Washington. This bill proposed the establishment of the National Research Foundation, with divisions concerned with support of research in various departments of science, including medicine, scholarships for promising science students throughout the nation and the promotion of international exchange of scientific information. A few days later a bill was introduced by Senator Kilgore, of West Virginia, proposing the establishment of the National Science Foundation, also committed to the desirable objectives just mentioned.

The differences in the organizational features of the two bills indicate why the Magnuson Bill re-

ceived the enthusiastic support of most of the scientists who testified at the hearings on both bills, which were held during October before joint Senate committees. Certain government officials, however, have expressed disapproval of the plan favored by the scientists. Alarmed by the potential dangers to the future of scientific research that they foresaw might result from significant modifi-

cations of the original Magnuson Bill, a group of scientists and educators comprising the Committee Supporting the Bush Report<sup>2</sup> recently addressed an open letter to President Truman. In this communication the principles on which they believe that sound legislation should be based are stated and certain features of the Kilgore Bill are adversely criticized.

In the first place, the men comprising this group emphasize that the Magnuson Bill is designed to implement the plan developed by the careful studies of Dr. Bush and his advisory committees. They are in favor of the provision of the Magnuson Bill that places the direction of the foundation in the hands of a board composed of laymen and scientists appointed by the President, with a full-time administrator appointed by and responsible to the board. They express opposition to the provisions of the Kilgore Bill for the appointment by the President of a single director, together with an advisory board, because they believe that the director "should be the agent — not the master — of the board." They point to what they regard as a further defect of the Kilgore plan, namely, the provision that calls for representation on the advisory board by *ex-officio* members responsible for the scientific programs of the Army, Navy and other governmental departments. This representation, they allege, would not make for a strong and impartial advisory board.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

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of going forward, since they are the ones in possession of the evidence — (*Ybarra v Spangard*, 154 Pac [2d] 687, Dec 27, 1944, rehearing denied Jan 25, 1945, California )

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### COMMUNICABLE DISEASES IN MASSACHUSETTS FOR DECEMBER, 1945

#### RÉSUMÉ

DISEASES	DECEMBER 1945	DECEMBER 1944	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	11	11	6
Chancroid	2	5	*
Chicken pox	900	1407	1511
Diphtheria	20	29	20
Dog bite	426	517	550
Dysentery bacillary	12	12	14
German measles	61	72	68
Gonorrhea	467	373	335
Granuloma inguinale	0	5	*
Lymphogranuloma venereum	0	2	*
Malaria	83	42	3
Measles	701	235	1082
Meningitis meningococcal	13	26	11
Meningitis, Pfeiffer bacillus	2	7	2
Meningitis pneumococcal	1	9	6†
Meningitis staphylococcal	1	0	0†
Meningitis streptococcal	0	0	0†
Meningitis other forms	3	1	2†
Meningitis undetermined	2	1	2†
Mumps	669	1352	670
Pneumonia lobar	165	232	396
Salmonella infections	5	5	5
Scarlet fever	523	1048	978
Syphilis	459	373	433
Tuberculosis pulmonary	172	171	239
Tuberculosis other forms	10	11	23
Typhoid fever	2	6	5
Undulant fever	10	3	3
Whooping cough	598	464	784

\*Made reportable December, 1943

†Four year average

#### COMMENT

Measles was reported less frequently during 1945 than during any year since 1907. During the month of December, however, there were three times as many cases as in December, 1944.

Scarlet fever was 50 per cent lower in December than it was during the corresponding month in 1944. In fact, from the months of August through December, 1945, the disease was reported less frequently than during a comparable period of months since 1940.

Cases of pneumonia were fewer than last year, in fact the number during December was lower than that for any December since reporting of pneumonia began in 1918.

#### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Billerica, 1, Boston, 2, Concord, 1, Lowell, 1, Manchester, 1, Pittsfield, 1, Somerset, 1, Winthrop, 1, Worcester, 2, total, 11.

Anthrax was reported from Franklin, 1, total, 1.

Diphtheria was reported from Belmont, 1, Boston, 8, Franklin, 1, Hingham, 1, Lowell, 1, Millville, 1, Monterey, 1, Peabody, 1, Sudbury, 1, Taunton, 2, Tyngsboro, 1, Wayland, 1, total, 20.

Dysentery, amebic, was reported from Camp Edwards, 1, Fort Devens, 1, Waltham Regional Hospital, 2, total, 4.

Dysentery, bacillary, was reported from Boston, 2, Braintree, 2, Cambridge, 1, Chelsea, 1, Lowell, 1, Waltham, 2, Wrentham, 3, total, 12.

Malaria was reported from Amherst, 1, Arlington, 1, Belmont, 1, Boston, 9, Brookline, 1, Cambridge, 1, Camp Edwards, 6, Chicopee, 1, Fort Devens, 31, Gloucester, 1, Hopedale, 1, Hull, 1, Lynn, 1, Medford, 1, Needham, 1, New Bedford, 1, Pittsfield, 1, Quincy, 1, Somerville, 2, Springfield, 1, Sutton, 1, Uxbridge, 1, Waltham, 1, Waltham Regional Hospital, 9, Wellesley, 1, Winthrop, 1, Worcester, 5, total, 83.

Meningitis, meningococcal, was reported from Adams, 1, Arlington, 1, Boston, 3, Great Barrington, 1, Lowell, 2, Nahant, 1, Somerville, 1, Springfield, 1, Waltham Regional Hospital, 1, Watertown, 1, total, 13.

Meningitis, Pfeiffer bacillus, was reported from Arlington, 1, Methuen, 1, total, 2.

Meningitis, pneumococcal, was reported from Worcester, 1, total, 1.

Meningitis, staphylococcal, was reported from Wrentham (State School), 1, total, 1.

Meningitis, other forms, was reported from Boston, 3, total, 3.

Meningitis, undetermined, was reported from Cambridge, 1, Haverhill, 1, total, 2.

Salmonella infections were reported from Cambridge, 1, Haverhill, 1, Malden, 1, North Andover, 1, Sheffield, 1, total, 5.

Septic sore throat was reported from Attleboro, 4, Boston, 3, Cambridge, 2, Fall River, 1, Medford, 1, Merrimac, 1, Williamstown, 1, total, 13.

Trichinosis was reported from Falmouth, 1, total, 1.

Typhoid fever was reported from Boston, 1, Methuen, 1, total, 2.

Undulant fever was reported from Adams, 1, Ashfield, 1, Brookline, 1, Fort Devens, 1, Hatfield, 1, North Andover, 2, Northampton, 1, Palmer, 1, Taunton, 1, total, 10.

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	February 1	Albert H Brewster
Salem	February 4	Paul W Hugenberger
Haverhill	February 6	William T Green
Brockton	February 14	George W Van Gorder
Worcester	February 15	John W O'Meara
Pittsfield	February 18	Frank A Slowick
Springfield	February 19	Garry deN Hough, Jr
Fall River	February 25	David S Grice
Hyannis	February 26	Paul L Norton

Physicians referring new patients to clinics should get in touch with the District Health Officer to make appointments.

## MISCELLANY

### CHANGES AT HARVARD SCHOOL OF PUBLIC HEALTH

Plans to increase the scope and importance of the Harvard School of Public Health were recently announced by President Conant. One of the world's foremost medical scientists, Brigadier General James Stevens Simmons, chief of the Preventive Medicine Service, Office of the Surgeon General, United States Army, has been appointed dean, succeeding Dr Edward G Huber, who has served as acting dean for the past several years. The Rockefeller Foundation has granted \$1,000,000 for expenses of the school from July 1, 1946, to June 30, 1956, and Harvard University has set aside a sum of \$750,000 to supplement the present endowment fund of the school.

In a reorganization intended to make this one of the outstanding research and teaching institutions in the world, the School of Public Health will have co-equal status with the Harvard Medical School and other professional divisions of the University. In addition to its present building at 55 Shattuck Street, Boston, the school will occupy the former Collis P Huntington Memorial Hospital. Acquisition of this nearby hospital, which is to be remodeled, will give the school an additional 40,000 square feet of floor space.

### SECTIONAL MEETINGS OF AMERICAN COLLEGE OF SURGEONS

The American College of Surgeons announces the resumption in 1946 of its sectional meetings, which during the war were replaced by one-day war sessions. Ten two-day meetings are planned, to begin in Minneapolis, with headquarters at the Radisson Hotel, on January 28 and 29. The second meeting will be held in the Hotel Jefferson, St Louis, on January 31 and February 1, the third at the Tutwiler Hotel, Birmingham, on February 8 and 9, the fourth in the William Penn Hotel, Pittsburgh, on March 11 and 12, the fifth at The Copley-Plaza, Boston, on March 18 and 19, the sixth in the

will produce a satisfactory measure. Scientists do not pretend to set themselves up as authorities on administrative procedure, but their own experience justifies their right to profess knowledge of the type of organization in which they would have confidence and of the particular conditions necessary to the most fruitful efforts of the research worker. Thus, what is wanted most of all in a national research foundation is not so much co-ordination by an efficient central organization but a means for *impartially discerning and aiding the all important*, but remote and often obscure, peripheral human units of the plan — those men and women whose curiosity about the phenomena of nature is truly compelling. The scientists are right when they say that in such persons lie the most important scientific resources of the Nation in peace, as has been so clearly shown to be the case in war.

#### REFERENCES

- 1 Bush V. Science — *The Endless Frontier* 184 pp. Washington D C Government Printing Office, 1945
- 2 Chambers, R. and Nicholas J. S. Pending legislation for federal aid to science. *Science* 102:545-548, 1945

### MASSACHUSETTS MEDICAL SOCIETY

#### DEATH

KNOWLTON — Edward A. Knowlton, M.D., of Holyoke, died August 22. He was in his sixty-third year.

Dr. Knowlton received his degree from Tufts College Medical School in 1909. He was senior visiting surgeon, Holyoke Hospital, visiting surgeon, Providence Hospital, and consulting surgeon to the Belchertown State School. He was former chairman of the Massachusetts Board of Registration in Medicine. He was a fellow of the American Medical Association and the American College of Surgeons.

### MEDICOLEGAL ABSTRACT

**Relation of Patient and Physician. Liability for malpractice.** Where a plaintiff is injured by an instrumentality entirely within the defendant's control under circumstances that would not arise unless someone had been negligent the courts apply the doctrine of *res ipsa loquitur*. The plaintiff by showing such circumstances raises a sufficient inference of negligence to go to the jury and, unless the defendant comes forward with a satisfactory explanation, to obtain a verdict. Various courts have made different applications of this doctrine — some strict, some liberal.

In a recent Arkansas case the plaintiff had a needle imbedded in her foot. The defendant examined her with a fluoroscope and performed an exploratory operation. About four or five days later the plaintiff's foot became inflamed.

The plaintiff sought to found her case on *res ipsa loquitur*. The court said that the fact that un-

favorable results do not ordinarily follow such a treatment does not raise an inference of malpractice by itself when unfavorable results do happen to occur. It went on to say that *res ipsa loquitur* does not apply to the practice of medicine and surgery or to the use of x-ray machines. Medicine and surgery are inexact sciences, and doctors are not guarantors of results. The implication of this last sentence is that *res ipsa loquitur* would only be applied where an injury raised an absolutely necessary inference that someone had been negligent. — (*Renton v. McGehee*, 186 S.W. [2d] 779, April 16, 1945, Arkansas.)

A somewhat different view of the doctrine was taken in a recent California case. The plaintiff was given a general anesthetic, and one of the defendants performed an appendectomy. When the plaintiff awoke he had a sharp pain in the right shoulder. After leaving the hospital this condition grew worse, he was unable to rotate his arm, and the arm became paralyzed and atrophied.

He brought suit against the doctor who had diagnosed his condition as appendicitis (the case is not clear whether this doctor was present at the operation), the doctor who performed the operation, the doctor who owned and operated the hospital, the anesthetist in the employ of the hospital and the special nurse who was in attendance after the operation.

The plaintiff introduced expert testimony to the effect that the paralysis was of traumatic origin. He then sought to invoke the doctrine of *res ipsa loquitur* to infer the defendants' negligence.

The trial court in entering a nonsuit as to all defendants found that there was no showing which defendant had control of the instrumentality causing the injury and that, since all defendants were not responsible for the acts of each other, the doctrine could not be applied. The plaintiff appealed and the judgment was reversed.

The court said that the unconscious patient is entitled to an explanation at least as much as the conscious pedestrian who is struck by an object coming from a building or other structure under the defendant's control. Concerning the relation of the various defendants, all of whom could hardly be held for a single act of negligence, the court found that all were temporary servants of the doctor performing the operation (*quere*) and that in any event the trial might absolve some of them from liability. Despite these difficulties the rule must be applied liberally so that those who were in a position to explain the injury are compelled to do so. Someone must in fact have been negligent and ought to be liable. The fact that the patient was unconscious and cannot identify the liable party does not deprive him of his rights. All the defendants were present for a common purpose.

The view taken here is that the doctrine applies because the defendants ought to have the burden

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## A TICK-BORNE EPIDEMIC OF TULAREMIA

LIEUTENANT COLONEL WILLARD B. WARRING, M.C., A.U.S., AND

MAJOR J. STERLING RUFFIN, JR., M.C., A.U.S.

BECAUSE tularemia has been generally regarded as a relatively infrequent disease, and because emphasis has been placed on its transmission by contact with animals, especially rabbits, an epidemic of 50 cases most of which were caused by tick bites is reported. These cases occurred among soldiers in the Tennessee maneuver area from March to December, 1943. Grouped according to the Hughes<sup>1</sup> classification of tularemia, these cases were divided as follows: ulceroglandular type, 35 cases; pulmonic type, 11 cases; glandular type, 3 cases; mixed ulceroglandular and pulmonic type, 1 case. All patients but 1 recovered.

Tularemia has been reported in every state of the Union except Vermont.<sup>2</sup> *Pasteurella tularensis* has been found in over twenty kinds of wild life.<sup>3</sup> Ticks, deer flies and cottontail rabbits are the three greatest sources of infection for man.<sup>4</sup> Transference of the disease between human beings has been reported.<sup>5</sup>

Although transmission of *P. tularensis* by several varieties of ticks has been demonstrated,<sup>3, 6, 7</sup> a survey of the area in which the present cases arose

were bivouacked in an area highly infested with ticks, and since *P. tularensis* can penetrate the unbroken skin,<sup>12</sup> it seems justifiable to assume that the ticks were the transmitting agents.

The onset of symptoms in the proved cases of tick bite occurred within one to twenty-one days. In 50 per cent of all cases the onset was acute. The outstanding symptoms were generalized aching, especially marked in the lumbosacral region and the lower extremities, headache, shaking chills, debilitating sweats, pain and tenderness in the regional lymph nodes, unproductive cough, weakness, dizziness, nausea, vomiting, anorexia and abdominal pain. In 5 cases, abdominal pain and tenderness, together with spasm of the abdominal muscles,

TABLE 2 Site of Primary Lesion

SITE	NO. OF CASES	PERCENTAGE
Arm, including hand	13	26
Upper two thirds of thigh and perineum	8	16
Lower abdomen	7	14
Leg, including foot	7	14
Buttocks	2	4
Scapular region	2	4
Buttocks region	2	4
Upper anterior chest wall	1	2
Unknown	8	16
Total	50	

TABLE 1 Incidence of Contact

NATURE OF CONTACT	NO. OF CASES	PERCENTAGE
Tick bite	32	64
Rabbit	5	10
Unknown probably contact with tick	13	26
Total	50	

revealed that all specimens were *Amblyomma americanum*, the so-called "lone-star tick."<sup>8, 9</sup> Parker<sup>10</sup> was unable to demonstrate *P. tularensis* from these ticks by culture, but previous studies in his laboratory had shown that the nymphs and larvae of *A. americanum* of the same generation transmitted *P. tularensis*.<sup>11</sup>

A definite history of tick bite prior to onset of illness was obtained in 32 of the 50 cases in this series (Table 1). Five appeared to be due to direct contact with rabbits. In 13 cases, a history of tick bite could not be obtained. Since these soldiers

suggested some acute disorder within the abdomen. Severe prostration was the rule. In 6 severely ill patients, marked delirium followed by drowsiness was present, the former being most marked in the pulmonic type of disease, which was also characterized by chest pain, unproductive cough and dyspnea out of proportion to the physical findings.

At the site of infection or bite were punched-out ulcers varying from 0.5 to 3 cm. in diameter. The edges were raised, irregular and surrounded by induration and erythema. The primary ulcers were found on the upper and lower extremities, perineum, buttocks, lower abdomen and scapular region (Table 2). In the majority of cases there was only one ulcer.



Mount Royal Hotel, Montreal, on March 22 and 23, the seventh at the Statler Hotel, Detroit, on March 26 and 27, the eighth in the Utah Hotel, Salt Lake City, on April 8 and 9, the ninth at the Multnomah Hotel, Portland, Oregon, on April 12 and 13, and the last in the Biltmore Hotel, Los Angeles, on April 17 and 18.

The medical profession at large, medical students and hospital executives are invited to join with the fellows of the College in these meetings. The invitation has been extended to the entire medical and hospital profession because only local meetings of medical groups have been held during the past three or four years and the College recognizes the need for disseminating information about new methods and therapies through larger meetings addressed by nationally prominent speakers.

## CORRESPONDENCE

### A CORRECTION

To the Editor In the July 12, 1945, issue of your journal, an item was published relating to a court case in Vermont where a decision was rendered involving a man by the name of Haskins, where suit had been brought for compensation for Christian Science treatment.

I believe it is only just to you and your readers to know that Haskins was never listed as a Christian Science practitioner in *The Christian Science Journal*, which is the organ of the Christian Science church containing a list of those who have the necessary qualifications to be recognized as authorized practitioners by The Christian Science Board of Directors. Although he was at one time a member of the Christian Science church, he is no longer a member.

It is true, as stated in your report, that "it is a violation of the rules of the church for a Christian Science practitioner to bring suit at law to recover for treatments given to a patient."

WM D KILPATRICK

Manager of Committees on Publication

The First Church of Christ, Scientist  
107 Falmouth Street  
Boston 15

## NOTICES

### ANNOUNCEMENTS

Dr. Leo Alexander announces his return from service in the United States Army and the opening of his office at 433 Marlborough Street, Boston, for the practice of psychiatry and neurology.

Dr. Joseph G. Cutler, having returned from overseas duty with the United States Army, announces the opening of his office at 397 Essex Street, Salem, for the practice of pediatrics.

### JOSEPH H PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9-10 a m

#### MEDICAL CONFERENCE PROGRAM

Friday, February 1 Diseases of the Orbit. Dr. Benjamin Sachs

Wednesday, February 6 — Obstetric Trends during the Last Five Years. Dr. Alonzo K. Paine

Friday, February 8 — Physiologic Evaluation of Quarter-master Clothing and Equipment. Colonel John H. Talbot

Wednesday, February 13 — The Treatment of Laennec Cirrhosis. Dr. Roy C. Crosby

Friday, February 15 — Diagnosis of Congenital Heart Disease by Venous Catheterization. Dr. Lewis Dexter

Wednesday, February 20 — Psychologic Aspects of the Menstrual Cycle. Dr. Norris T. Flanagan

Friday, February 22 — Holiday

Wednesday, February 27 — Practical Aspects of Ringworm Diseases. Dr. Ernst Bernhardt.

On Tuesday and Thursday mornings, Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek.

All morning conferences are open to the medical profession.

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, February 7, in the classroom of the Nurses' Residence at 7:15 p m. Dr. Siegfried Thannhauser will discuss an interesting case of jaundice. Dr. Helena M. Murphy will be chairman.

## UROLOGY AWARD

The American Urological Association offers an annual award, not to exceed \$500, for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deems none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the secretary for full particulars. The selected essay (or essays) will appear on the program of the meeting of the American Urological Association to be held at the Netherland Plaza, Cincinnati, July 22 to 25. All essays must be in the hands of the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before July 1.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JANUARY 31

#### FRIDAY, FEBRUARY 1

- \*9:00-10:00 a m Medical clinic. Isolation Amphitheater Children's Hospital
- \*9:00-10:00 a m Diseases of the Orbit. Dr. Benjamin Sachs. Joseph H. Pratt Diagnostic Hospital
- \*10:00 a m-12:00 m Medical staff rounds. Peter Bent Brigham Hospital
- 10:50 a m Postgraduate clinic in dermatology and syphilology. Amphitheater. Dowling Building. Boston City Hospital

#### MONDAY, FEBRUARY 4

- \*12:00 m-1:00 p m Clinicopathological conference. Peter Bent Brigham Hospital

#### TUESDAY, FEBRUARY 5

- \*9:00-10:00 a m Medical clinic. Infants Hospital
- \*12:15-1:15 p m Clinicoradiological conference. Peter Bent Brigham Hospital

#### WEDNESDAY, FEBRUARY 6

- \*9:00-10:00 a m Obstetric Trends during the Last Five Years. Dr. Alonzo K. Paine. Joseph H. Pratt Diagnostic Hospital
- \*12:00 m Clinicopathological conference. Children's Hospital

\*Open to the medical profession

JANUARY 7-APRIL 22 1946 Metropolitan State Hospital. Eleventh postgraduate seminar in neurology and psychiatry. Page 314, issue of September 6.

JANUARY 30 Arlington Doctors Club and Belmont Medical Club. \$2.00 p m Ring Sanatorium and Hospital.

FEBRUARY 1-27 Joseph H. Pratt Diagnostic Hospital. Medical conference program. Notice above.

FEBRUARY 2 American Board of Obstetrics and Gynecology. Page 514, issue of October 25.

FEBRUARY 4-MARCH 29 Health Education Institute. Page 746, issue of December 13.

FEBRUARY 7 New England Hospital for Women and Children. Notice above.

FEBRUARY 9 New England Dermatological Society. Page xix, issue of January 17.

FEBRUARY 13 Massachusetts Medico-Legal Society. Page xix, issue of January 17.

FEBRUARY 14 Diagnostic and Therapeutic Suggestions in Cardiovascular Disease. Dr. John Sproull. Pentucket Association of Physicians. 8:30 p m. Haverhill.

FEBRUARY 20 Tufts Medical Alumni Lecture. Page xix, issue of January 17.

MAY 13-17 American College of Physicians. Page 798, issue of December 20.

## DISTRICT MEDICAL SOCIETY

### WORCESTER

- FEBRUARY 13 Worcester State Hospital
- MARCH 13 Worcester Memorial Hospital
- APRIL 10 Hahnemann Hospital
- MAY 8 Annual meeting

previous day he had removed from his right thigh a tick that had been present for an unknown period of time

Physical examination revealed an acutely ill man with a small punched-out ulcer on the anterior aspect of the right upper thigh and enlarged, smooth, discrete lymph nodes measuring between 2 and 4 cm in diameter in the right inguinal region

Fever varying between 101.8 and 104°F continued for 12 days, after which remissions occurred for 6 days, with a gradual decline by lysis to normal levels. The white-cell count varied from 6250 to 11,400. Repeated dark-field examination of material from the ulcer, the Frei test, the Kahn test and urinalyses were all negative. Culture from the ulcer showed a nonhemolytic *Staphylococcus albus*. The serum agglutination titer for tularemia on the 20th day was 1:10,240.

Convalescence was uneventful. At the end of 30 days the ulcer had healed and the inguinal nodes were nontender, although still enlarged. The patient was discharged to duty complaining of slight weakness.

**CASE 2** A 30-year-old soldier was admitted to an evacuation hospital on May 28, 1943, complaining of generalized

On July 29, the patient was transferred to another station hospital and thence to a general hospital and finally to another general hospital. During this interim the ulcer had healed, but the right axillary nodes had become more enlarged and had gradually softened. A thick, greenish exudate was removed from these nodes by aspiration on several occasions.

At the latter general hospital, 3300 units of penicillin was injected into one of the abscess cavities after aspiration, but this appeared to make the abscess worse. By October 11 the abscess had healed. The agglutination titer on August 27 was 1:1282. Because of weakness, the patient remained in bed until October 27. Later he was placed in a group participating in a reconditioning program. The total hospitalization period was 203 days.

*Mixed Ulceroglandular and Pulmonic Type*

**CASE 3** A 24-year-old soldier was admitted on June 18, 1943, complaining of generalized aching, headache, malaise, fever, sweating, colicky abdominal pain, and diarrhea of 2 days' duration. He had removed ticks from his body on several occasions during the previous 2 weeks.

Physical examination revealed an acutely ill, oriented

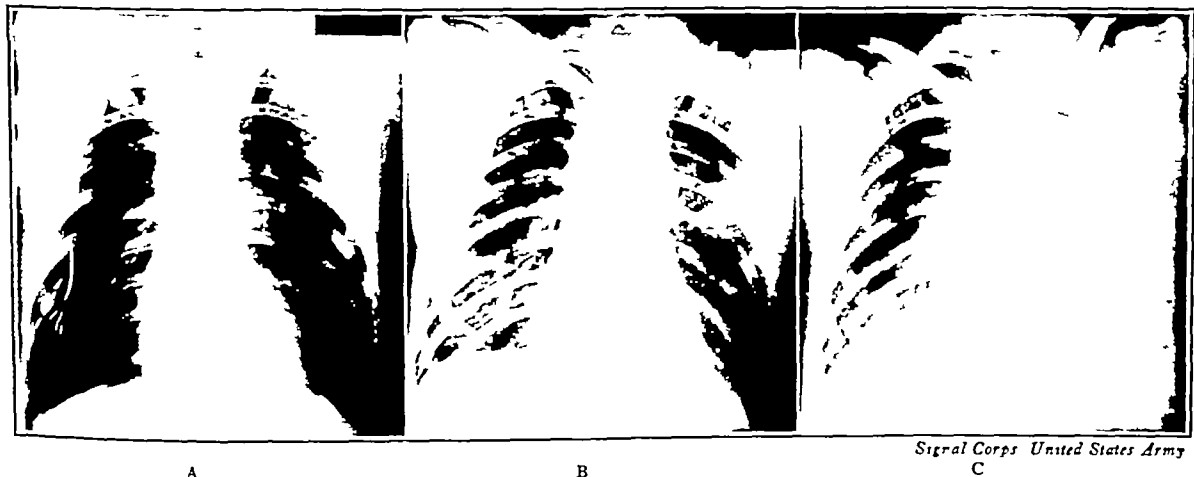


FIGURE 1 Case 3

The interpretations of these bedside x-ray films were as follows: A (7-19-43) "There is hilar adenopathy, on the left. The lung fields are too dark to reveal any interstitial changes"; B (7-21-43) "There is a considerable amount of peribronchial infiltration in the right base. There is a small area of consolidation in the region of the third interspace on the left. The mediastinum appears to be widened and irregular"; C (7-24-43) "There is a massive pleural effusion involving the left chest, but lung markings are seen in the upper third. The hilar adenopathy appears to be practically the same as that in the previous films. The infiltration in the right base has slightly cleared. The mediastinum is widened."

aching, headache, fever, chills, sweats, backache and slight stiffness of the neck. Two days previously a tick had been removed from the right arm. Physical examination was negative except for a temperature of 100°F.

On June 7, the patient was transferred to a station hospital because of fever of undetermined origin. He was acutely ill, and his previous symptoms had become exaggerated. Moreover, the patient presented signs of cerebral irritation, which was manifested by restlessness, irritability and mental confusion. The temperature on this admission was 105.4°F. Physical examination showed a small punched-out ulcer on the right forearm just distal to the elbow, enlarged, tender lymph nodes in the right axillary region, slight nuchal rigidity and abdominal distention. The white-cell count was 13,000. The results of spinal-fluid examination were within normal limits. An agglutination test for tularemia on blood taken at the time of admission was negative. On June 8, a discrete, red, macular rash appeared on the trunk and arms. The abdominal distention became more marked, and the patient vomited moderate amounts of a coffee-colored material and became stuporous. For 8 days there was continuous fever ranging between 103 and 105°F, but on the 14th day the temperature began to drop by lysis and symptoms gradually subsided. On June 15, the agglutination titer for tularemia was 1:1280.

patient with a temperature of 103.6°F and marked tenderness over the right costovertebral angle. The white-cell count was 10,700. The urine gave a +++ test for albumin.

On July 21, an unproductive cough and pain on inspiration developed in the lower right chest. The patient appeared critically ill and was cyanotic and dyspneic. Physical examination and x-ray examination of the chest revealed signs of consolidation in the right lower lobe and a widened mediastinum (Fig 1B). The pneumonic process rapidly progressed until it involved almost all the left lung and the middle and lower lobes of the right lung. A pleural effusion developed in the left side of the chest (Fig 1C). The spleen was palpated 2 fingerbreadths below the left costal margin. The temperature varied between 101.2 and 105.4°F. The patient became delirious, and the prostration, dyspnea, and cyanosis increased. Blood, stool and urine cultures were negative. Repeated sputum examinations were negative for acid-fast bacilli. On the 6th day of the disease, the white-cell count was 6750 and remained at this level until the death, which occurred on the 10th day.

**Autopsy** The significant post-mortem findings were as follows: The left chest contained 1000 cc. of cloudy, straw-colored fluid, in which were flecks of yellow fibrinous material. Findings consistent with pneumonia were present in the entire left lung and the lower lobe of the right lung. In addition, in the left upper lobe there were many indurated areas, which

Enlarged regional lymph nodes, single or multiple, and varying from 2.5 to 6 cm in diameter were found in every case with an obvious primary lesion and in 3 without one. The nodes were at first nontender, but as they increased in size they became tender and fluctuant and the overlying skin became reddish purple and thin. If not incised, these nodes usually suppurated and drained. In 38 cases with nodular involvement, the nodes were suppurative in 35 and nonsuppurative in 3. In 6 cases, nodes in other areas enlarged simultaneously with regional nodes draining the affected area, they slowly resolved without softening.

In 8 cases, a diffuse, erythematous, maculopapular eruption, distributed over the entire body but most pronounced over the extremities, appeared between the fifth and eleventh days of the disease. In 2 cases, it was morbilliform. The average duration of the eruption was eight days.

Two cases with acute fibrinous pleurisy and 3 with pleural effusion were encountered in the ulceroglandular type. In the pulmonic type, findings consistent with pneumonia were present. In the more serious of these cases, there appeared definite areas of consolidation involving one or several lobes, accompanied by cyanosis and dyspnea. Resolution of the pneumonia began in the third week and was extremely slow, requiring from five weeks to six months for completion.

Between the second and the fourth week, pleural effusion occurred in 9 of the 11 patients with pure pulmonic involvement. After repeated thoracenteses, the effusion subsided in ten days to five months, with an average of seventy-five days. The fluid was either greenish or serosanguineous, its specific gravity varied from 1.015 to 1.022 and the predominating cells were lymphocytes. Direct smears showed no organisms.

In 1 case, severe dyspnea was caused by a mass in the mediastinum, which gradually increased in size. The patient died on the tenth day of illness, and at autopsy the mediastinum was filled with enlarged lymph nodes.

In early stages of the disease, fever was continuous, varying between 101 and 105°F. Later there were morning remissions, and in the majority of cases the fever fell by lysis to normal in the fourth week of the disease. In patients with pleural effusion, thoracentesis caused a drop in temperature and a decrease in respiratory embarrassment.

The primary skin lesion healed with scar formation in four to seven weeks.

The patient's reaction varied from mild constitutional symptoms to marked prostration, depending on the severity of the disease. Convalescence was slow. Weakness, lassitude and loss of weight persisted for an indefinite period of time. Most of the patients have been in the hospital for three to six months and are still convalescing.

There was nothing significant in the white-cell

counts, since they varied from normal to 15,150. The differential count revealed a slight shift to the left.

In all 50 cases, diagnosis was confirmed by agglutination tests which were positive in dilutions of serum varying from 1:320 to 1:10,240. The agglutinins were usually present in the second or third week of the disease, and the highest titers were reached between the third and the eighth week—a fact that is of diagnostic significance. Cross agglutination occurred in 5 cases with *Brucella abortus* and in 1 case with *Proteus* OX 19. All were excluded by the laboratory procedure in which a tularemic serum agglutinates a suspension of *P. tularensis* more rapidly and to a higher titer than it does *Br. abortus*, *Br. melitensis* or *Proteus* OX 19 antigens.<sup>3</sup>

Cultures made from the pleural exudate on the usual laboratory mediums to exclude the presence of pathogenic bacteria were negative. Smears of material from the ulcers, suppurating nodes and sputum revealed no *P. tularensis*. Guinea pigs were inoculated but unfortunately died of some other infection that became epidemic in the animal house.

The treatment was nonspecific and supportive. Oxygen given early to patients with pneumonia and continued throughout the acute stage seemed to offer the best chance for recovery. Wet dressings and bland ointments were applied to ulcerated lesions. When softening of regional nodes occurred, surgical incision and drainage were instituted. Thoracentesis performed in cases with pleural effusion caused an amelioration of symptoms. Administration of sulfathiazole and sulfadiazine was without apparent benefit.

Diseases with which tularemia may be readily confused include sporotrichosis, actinomycosis, meningitis, typhoid fever, Rocky Mountain spotted fever, acute infectious mononucleosis, lymphogranuloma inguinale, typhus fever, pneumonia, measles, tuberculosis, malaria and undulant fever.

The laboratory methods of confirming the diagnosis are three in number—growth of the organism from the blood or pleural or spinal fluid on a blood cysteine agar medium, inoculation of guinea pigs with this material and repeated serum agglutination tests.<sup>6</sup> The agglutination test is regarded as one of the most reliable confirmatory tests in the field of serology.<sup>3</sup> Ransmeier and Ewing<sup>13</sup> have shown that a positive tularemic agglutination titer may persist for a number of years. We have had no experience with Foshay's<sup>14</sup> intradermal test.

The following cases are representative of the various types of tularemia that were encountered.

#### CASE REPORTS

##### Ulceroglandular Type

CASE 1. A 22-year-old officer was admitted to the hospital complaining of generalized aching, chills and fever. The

# PENICILLIN IN THE TREATMENT OF BRONCHIECTASIS\*

## A Preliminary Report

I D BOBROWITZ, M D,† JAMES S EDLIN M D,‡ SYDNEY BASSIN, M D,§ AND

J STANLEY WOOLLEY, M D ¶

OTISVILLE, NEW YORK

**R**EPORTS on the use of penicillin in the treatment of pleural and pulmonary suppurative conditions are appearing in increasing numbers. A favorable response has been achieved in acute pneumonitis<sup>1-4</sup> and pulmonary abscess.<sup>2, 3</sup> The best effects have been obtained in infections caused by streptococci, staphylococci, pneumococci and actinomyces, and the poorest in those with mixed anaerobic bacteria. These cases were treated by intravenous or intramuscular administration of the drug. Penicillin has also been utilized satisfactorily in hemothorax to prevent infection.<sup>2, 5</sup> Acute pyogenic empyemas have been cleared of organisms and the toxemia prevented or reduced.<sup>2, 4-6</sup> by aspiration of chest fluid and the intrapleural instillation of penicillin. Mixed-infection empyemas have been similarly treated.<sup>2, 5</sup> to prepare patients for thoracoplasty.

White et al.<sup>7</sup> used penicillin in the prevention of postoperative empyema following lung resection. Forty-one patients had pneumonectomy or lobectomy for bronchiectasis, lung abscess, tuberculosis or neoplasm. Twenty-one of them received 150,000 units of penicillin daily — 12,500 units intramuscularly every two hours — for one week preoperatively and for two weeks postoperatively, and 20 patients served as controls. None of the penicillin-treated patients developed empyema, whereas 12 or 60 per cent of the controls did so. Penicillin was given to 12 patients with lung resection for bronchiectasis and multiple lung abscesses. Five of them had a reduction in sputum volume before operation, and 2 had a thinning and decrease in purulence of sputum. In 6 cases, penicillin given in experimental cases for seven days before operation caused hemolytic streptococci to disappear from the sputum soon after therapy was instituted. Pneumococci and streptococci were usually unaffected, although in an occasional case these organisms disappeared. Gram-negative bacilli frequently occurred and often persisted throughout the period of hospitalization. The bronchial secretions of 2 patients were tested for the presence of penicillin, and none was detectable in either. Blood samples revealed varying concentrations of penicillin. These authors believe that the preoperative administration of penicillin serves to control acute and chronic infection in the pul-

monary tissues. This reduces the possibilities of postoperative infections and affords a maximum drug effect at the time the pleural space is exposed to bronchial contamination.

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The present study was made to determine the value of penicillin in the treatment of bronchiectasis. Various modes of administration were utilized — intramuscular, intratracheal or intrabronchial and inhalation (nebulization) and combinations of these methods. It was particularly planned to estimate the advantages of the topical or bronchial effect of the drug.

The treatment was given to 12 patients — 10 men and 2 women — 2 of whom were Negroes. The ages varied from sixteen to thirty years. Therapy was initiated in the first case on August 9, 1944 and in the last one on April 18, 1945. The first nine patients were treated at the Municipal Sanatorium, Otisville, New York, and the last three at St. Clare's Hospital, New York City. All patients followed up were seen at the St. Clare Clinic.

## PLAN OF STUDY

For a few days to a week or more prior to penicillin administration and throughout the hospitalization period, the patients were kept on postural drainage — two or three times a day for ten to fifteen minutes. When the penicillin was administered intratracheally, postural drainage immediately preceded the treatment to improve the topical action of the drug. This procedure also facilitated the collection of the sputum and assured a satisfactory total daily output. The patients were instructed to continue postural drainage after discharge.

The sputum was examined frequently and often daily before, during and after treatment, the twenty-four-hour amount being carefully determined either by measure or by weight, and the presence or absence of odor was noted. A gram-stained smear was made of each specimen received, — in twenty-four-hour collections, — and the presence and relative number and kinds of organisms were noted. A Fontana-stained smear was examined for each of the Otisville patients. Sputum cultures were done from time to time.

The sputum in established bronchiectasis usually exhibits a highly diversified flora that includes gram-positive and gram-negative organisms. Since the

\*From the Municipal Sanatorium, Otisville, New York, one of the institutions of the Department of Hospitals, City of New York.

†Medical superintendent, Municipal Sanatorium.

‡Visiting physician, Municipal Sanatorium.

§Associate visiting physician, Municipal Sanatorium.

¶Director of laboratory, Municipal Sanatorium.

were nodular in form and consisted of necrosis and caseation. The nodules varied from 1.5 to 3.0 cm in diameter. The mediastinum contained large masses of purple-black, firm, enlarged lymph nodes, varying from 1.5 to 4.0 cm in diameter. They were anterior to the esophagus and extended to the hilar region of each lung. All showed areas of necrosis and caseation. All the viscera, including the brain, showed moderate congestion. Both the spleen and the liver were markedly enlarged. The spleen showed necrosis and cell fragmentation, and the liver contained areas of abscess formation. Blood taken from the heart revealed a positive tularemia agglutination titer of 1:320.

#### Pulmonic Type

**CASE 4** A 23-year-old officer was admitted on October 9, 1943, complaining of generalized aching, chills, fever and unproductive cough. During the previous 10 days he had been bitten by many unidentified insects. Since he had been billeted in a tick-infested area, it seemed probable that some of the bites had been by ticks.

Physical examination revealed a prostrated man with a temperature of 103°F, multiple insect bites over the entire

to be characteristic of the disease, especially in cases with a definite primary lesion. Convalescence is prolonged. The agglutination test is considered the most reliable diagnostic test for tularemia.

Some representative cases of the various types of tularemia encountered in this series of 50 cases are reported.

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Signal Corps, United States Army

FIGURE 2 Case 4

The interpretations of these x-ray films were as follows: A (10-12-43) "There is an area of consolidation in the left upper lobe in the region of the second and third interspaces that resembles a lobar pneumonia" (this film was made in a field hospital with field equipment at a distance less than 72 inches, which explains the distortion of the cardiac shadow); B (10-17-43) "There remains a considerable amount of infiltration in the same area, with a small area of decreased density lying just above the end of the second rib, which appears to be cavitation"; C (2-7-44) "The lung fields have almost cleared. Only a small fibrotic area at the end of the second rib remains."

trunk and extremities, consolidation of the upper lobe of the left lung and moist rales over the lower lobe of the right lung. A roentgenogram of the thorax showed a diffuse infiltration in the upper left lobe (Fig. 2A).

On the 5th day, the temperature was 99.4°F, and it continued intermittently at this level for 7½ months. The blood agglutination titer for tularemia was 1:2560 on November 6 and 1:640 on January 7, 1944. After 225 days of hospitalization, the patient still complained of weakness, malaise and slight discomfort in the left upper chest. Serial roentgenograms revealed a gradual clearing of the pneumonic process in the left upper lobe. At the end of 7½ months, however, it was still undetermined whether this area represented a continued infiltrative process or fibrotic changes (Fig. 2C).

#### SUMMARY

Ticks are important carriers of *Pasteurella tularensis*. Enlargement of regional lymph nodes seems

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The dosage of penicillin and the methods of administration are shown in Table 1. The intramuscular doses were given in a concentration of 1000 units per cubic centimeter of physiologic saline solution. In all the intratracheal cases except Case 7 the penicillin was administered by the supraglottic method preceded by topical cocaine. In Case 7, an intrabronchial catheter was used for three days and an intratracheal catheter for nine days but otherwise the usual supraglottic route was utilized. During all these intratracheal instillations the patient was placed so that the drug could reach the affected lobes. Each dose was dissolved in 10 to 20 cc of saline solution. The inhalation method consisted in nebulization of the penicillin solution in a vaporizer. The technic employed was that previously described.<sup>9</sup> In the Otisville cases, however, a glass Y connection was placed on the tube leading from the oxygen tank to the

Of the 10 patients with a foul sputum, in 9 the odor completely cleared and in 1 it slightly diminished. The former effect was achieved within one day in 4 patients — intratracheal administration in 2, inhalation in 1, and intramuscular and intratracheal administration in 1, within forty-eight hours in 3 cases — intramuscular administration, intratracheal injection, and intratracheal injection and inhalation each in 1, and after intervals of three and six days the 2 other cases — (inhalation in 1 and intratracheal administration and inhalation in 1). Whenever the offensive smell of the sputum disappeared after penicillin, the effect continued throughout the period of therapy. In 3 cases the treatment is still being continued. The odor returned following discontinuation of penicillin in 3 patients after intervals of three days, four days and three months, respectively. Two patients had no recurrence of odor but the followup lasted for only eight days in one and one month in the other. Sufficient time has not elapsed to deter-

TABLE 2 Changes in Amount of Sputum after Penicillin Therapy

CASE NO	METHOD OF ADMINISTRATION	BEFORE PENICILLIN AMOUNT	AFTER PENICILLIN		SPUTUM LEVEL AFTER CESSATION OF TREATMENT
			AMOUNT	RAPIDITY OF EFFECT	
1	Intramuscular and intratracheal injection	160-240 cc	4 cc	6 days	60 cc (2 mo) 120 cc (3 1/2 mo)
2	Intramuscular injection	60 cc	18 cc	2 days	Patient left against advice
3	Intratracheal injection	45-60 cc	22 cc	2 days	15 cc (3 wk) 30 cc (1 mo and 3 mo)
4	Intratracheal injection	300 cc	0 cc	3 days	40 cc (1 wk) 70 cc (3 and 4 wk)
5	Intratracheal injection	90 cc	40 cc	4 days	42 cc (6 1/2 mo)
6	Intratracheal injection	120 cc	40 cc	4 days	80 cc (1 wk) 55 cc (3 wk and 6 1/2 mo)
7	Intratracheal injection	207 gm	105 gm	4 wk	No followup
8	Inhalation	29 gm	11 gm	4 wk	20 gm (4 mo)
9	Inhalation	145 gm	0 gm	4 wk	79 gm (8 days)
10	Intratracheal injection and inhalation	180-240 cc	16 cc	5 days	Treatment continued
11	Intratracheal injection and inhalation	70 cc	14 cc	9 wk	Treatment continued
12	Inhalation	110 cc	23 cc	4 days	Treatment continued
			10 cc	6 wk	
			28 cc	6 days	Treatment continued
			12 cc	7 wk	

vaporizer and controlled by the patient's closing or opening the open end with his finger. When the connection was open, the oxygen passed through the Y tube to the outside and not to the nebulizer and the patient was able to rest. When it was closed, the oxygen passed to the vaporizer forming a penicillin mist or vapor, which was inhaled. An L-shaped glass extension was also connected to the stem of the vaporizer, which dipped down behind the base of the tongue so that the penicillin spray could be directed toward the larynx. Each dose was dissolved in 2 to 4 cc of saline solution.

There were no real difficulties in administering the drug. Three of the patients receiving intratracheal administration (Cases 4, 5 and 6) experienced slight nervousness and sleeplessness as the result of the cocaine. Use of the intrabronchial catheter was soon discontinued, since it appeared to be irritating. In 1 patient (Case 8) treated with inhalation therapy, a dermatitis occurred on the face and lips. This was relieved by a vaseline ointment without discontinuation of therapy. A skin test and a patch test with penicillin were both negative.

mine the lasting effect of the drug in these cases. One patient left the hospital against advice, and there is no information on the present status of his sputum.

The changes in the sputum volume are shown in Table 2. The figures covering the penicillin effect on the total twenty-four-hour sputum amount represent the lowest sputum level that was steadily maintained and the time during the period of treatment at which it occurred. Actually there was a progressive diminution in sputum output, which started as soon as treatment was begun, but the maximum reduction took place at variable periods after the treatment was initiated. As indicated by the table, this required from a few days to several weeks. The patients treated by intratracheal instillation in all cases but 1 showed the maximum effect within a few days. The inhalation cases and those with combined intratracheal injection and inhalation treatment showed a significant early reduction, but the most marked diminution required several weeks. In every patient but the one who left against advice, the sputum reduction was at least 50 per cent. For

action of the penicillin is exerted chiefly on the former, their presence or absence in the smear constituted a practical index of the effectiveness of the penicillin, the reliability of which was borne out by the occasional cultures. In 8 patients, bioassays of the penicillin content of the sputum, urine and blood were frequently done — in some cases daily — during and after the administration of the drug and were continued until it disappeared from the specimens. The method described by Woolley and Schmidt,<sup>8</sup> an adaptation of the Fleming agar-hole method, was employed. With this procedure, contaminated material can be readily assayed and blood serums measured. Although the sensitivity of the test organism (*Staphylococcus aureus* "H")

lobe was involved in 12 cases, the right lower lobe in 9, and the right middle lobe and lingula portion of the left upper lobe in 6 each. Of the thirty-three bronchiectatic lobes, a marked saccular condition was present in nineteen, a moderate saccular involvement in three, moderate cylindrical and varicose dilatations in six, and slight cylindrical enlargement in five. In addition, bronchiectasis existed in two lobes that were atelectatic.

The onset of symptoms followed pneumonia in 10 cases, pertussis in 1 and influenza in 1. The symptoms had existed for four to twenty-four years, with a duration of more than ten years in all but 2 cases. In 7 cases, pneumonic episodes had recurred, and in 2 of these they had done so two and

TABLE 1 Dosage and Method of Treatment

CASE No	METHOD OF ADMINISTRATION	DURATION OF TREATMENT days	DOSAGE	TOTAL DOSAGE units
1	Intramuscular and intratracheal injection	12	100,000 units a day 80,000 intramuscularly (10,000 every 3 hours) and 20,000 intratracheally	1,200,000
3	Intramuscular injection	5½	100,000 units a day alternating 10,000 and 15,000 every 3 hr	550,000
2	Intratracheal injection	10	100,000 units a day 50,000 twice daily	1,000,000
4	Intratracheal injection	4	250,000 units a day 100,000 in morning, 150,000 in afternoon	1,000,000
5	Intratracheal injection	4	250,000 units a day 100,000 in morning, 150,000 in afternoon	1,000,000
6	Intratracheal injection	4	250,000 units a day 100,000 in morning, 150,000 in afternoon	1,000,000
7	Intratracheal injection	30	50,000 units a day	1,500,000
8	Inhalation	30	50,000 units a day 10,000 every 3 hours for five doses	1,500,000
9	Inhalation	60	100,000 units a day for first 20 days 20,000 every 3 hours for 5 doses, then 50,000 units a day for 40 days 10,000 every 3 hours for five doses	4,000,000
10*	Intratracheal injection and inhalation	105	100,000 units a day intratracheally for 10 days then 100,000 units three times a week by inhalation (100,000-unit doses) for 95 days	4,900,000*
11*	Intratracheal injection and inhalation	115	100,000 units a day intratracheally for 10 days then 100,000 units three times a week by inhalation (100,000-unit doses) for 105 days	5,500,000*
12*	Inhalation	60	100,000 units a day for 10 days then 100,000 units three times a week	3,100,000*

\*Patient still under treatment

employed in this method is insufficient to determine accurately amounts less than 0.2 units per cubic centimeter, the method was considered adequate because penicillin in lower concentrations is ineffective against some organisms — staphylococci and so forth. From necessity, containers for sputum and urine were kept refrigerated at all times in ice buckets near the patients' beds so that as little of the penicillin effect as possible would be lost. The amount of active penicillin per cubic centimeter for each specimen was determined, and from this the twenty-four-hour elimination was estimated.

## RESULTS

The diagnosis was made in every case by means of a bronchogram with lipiodol. The bronchiectasis was multilobar in all 12 cases and bilateral in 11. Two lobes were involved in 4 cases, three in 7, and four in 1. In other words, the 12 patients had thirty-three bronchiectatic lobes. The left lower

lobe was involved in 12 cases, the right lower lobe in 9, and the right middle lobe and lingula portion of the left upper lobe in 6 each. Of the thirty-three bronchiectatic lobes, a marked saccular condition was present in nineteen, a moderate saccular involvement in three, moderate cylindrical and varicose dilatations in six, and slight cylindrical enlargement in five. In addition, bronchiectasis existed in two lobes that were atelectatic.

The onset of symptoms followed pneumonia in 10 cases, pertussis in 1 and influenza in 1. The symptoms had existed for four to twenty-four years, with a duration of more than ten years in all but 2 cases. In 7 cases, pneumonic episodes had recurred, and in 2 of these they had done so two and

three times, respectively, only 1 patient had a co-existent tuberculosis, and in this case it had been present in both upper lobes for six years. The symptoms and physical findings were those characteristic of this condition. In addition, 2 cases gave radiographic evidence of sinus involvement. The sputum showed varying degrees of purulence. In all but 2 cases it had a foul odor and in most cases it separated on standing into the characteristic three layers. All the specimens exhibited a more or less similar bacterial flora. The more putrid they were, the greater were the number of organisms. Gram-positive organisms predominated in all smears: chains (streptococci) were present in 9 patients, grape-like clusters (staphylococci) in 8, diplococci in 8 and rods in 2. The gram-negative organisms included fusiform bacilli in 5 patients, biscuit-shaped diplococci (*Micrococcus catarrhalis*) in 4, rods in 3, cocci in 2, and diplococci in 1. No spirochetes were found with the Fontana stain. The sputum cultures verified the findings of the sputum

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4	Intratracheal injection	300 cc	90 cc	1 day	40 cc (1 wk) 70 cc (3 and 4 wk)
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9	Inhalation	145 gm	50 gm	4 wk	79 gm (8 days)
10	Intratracheal injection and inhalation	180-240 cc	36 cc	5 days	Treatment continued
			14 cc	9 wk	
11	Intratracheal injection and inhalation	70 cc	23 cc	4 days	Treatment continued
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			12 cc	7 wk	

vaporizer and controlled by the patient's closing or opening the open end with his finger. When the connection was open, the oxygen passed through the Y tube to the outside and not to the nebulizer and the patient was able to rest. When it was closed, the oxygen passed to the vaporizer, forming a penicillin mist or vapor, which was inhaled. An L-shaped glass extension was also connected to the stem of the vaporizer, which dipped down behind the base of the tongue so that the penicillin spray could be directed toward the larynx. Each dose was dissolved in 2 to 4 cc of saline solution.

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the entire group, excluding those still under treatment, the average was 63 per cent. It is possible that the postural drainage itself accounted for some diminution in sputum. The best effect has thus far been shown in patients receiving combined intratracheal injection and inhalation therapy. In the patients followed up for periods averaging over three months, however, cases with an increase in sputum output occurred after treatment was discontinued. In 2 of the cases with intratracheal administration, the sputum continued to diminish for a short time (one to three weeks) before it increased. In no case did it return to its original level present before therapy, and usually it continued at only half of the pretreatment amount. Since postural drainage and the collection of sputum cannot be so well controlled after discharge from the institution, the expectoration may have been greater than that reported by the patients.

As would be expected, the penicillin tended to clear the sputum of organisms, especially the gram-positive ones, with rapidity. As a result of this, the pus cells were materially reduced. In 7 cases, all gram-positive organisms disappeared completely from the sputum. This was achieved by every method of administration, except in the patient given penicillin intramuscularly who left against advice. In the intratracheally treated cases, this effect occurred within two or three days, whereas in those treated by inhalation it required a week or two. In 3 patients, the gram-positive bacteria were eliminated within one or two weeks, but a few reappeared while treatment was continued. In 2 cases, including that of the patient incompletely treated, occasional gram-positive organisms remained.

Gram-negative organisms were also favorably influenced by the treatment. In 4 cases, — 3 treated intratracheally and 1 by inhalation, — they disappeared. With the intratracheal injection, this occurred within two to four days, and with inhalation at the end of two weeks. In the other cases a rare or occasional number of gram-negative organisms persisted.

In every case there was a decrease in the purulence of the sputum, and usually only a few cells remained. As with the bacterial changes, the intratracheal injection produced the maximum effect in a few days, and inhalation technic in one or two weeks.

In all patients followed up, there was a rapid change in the bacterial content and purulence of the sputum as soon as the penicillin was discontinued. In 5 of the 8 patients with a completed course of treatment, gram-positive organisms appeared or increased within two to five days after the penicillin was stopped and continued to multiply. In 3 cases, — all treated intratracheally, — the organisms appeared or increased after an interval of one or two weeks and later became more numerous. In 6 patients, gram-negative organisms re-

appeared or increased, either in a few days or a few weeks.

In every case the sputum also became more purulent when the penicillin was stopped. This took place either within a few days or after a week or two.

There was symptomatic improvement in every patient. Cough was rapidly alleviated, and in all but 2 patients the effect became evident within a few days. The cough decreased to the point where expectoration took place with postural drainage only. Night coughing almost ceased, and the stimulation to cough formerly caused by exertion, laughter, deep breathing or change in position no longer occurred. Dyspnea was much reduced, and in 1 patient it was eliminated. Wheezing and chest heaviness were also relieved. Anorexia was improved. Six patients gained weight while under treatment, and 4 of these continued to do so after penicillin was discontinued. Significantly, several of these patients had been markedly under weight for many years. Two of the patients began to gain after treatment. A slight loss of weight occurred in 3 patients, 2 of whom had had a normal weight before admission. One patient showed a marked reduction in nasal discharge. Incidentally, in 1 case with a pustular acne of the face the condition entirely cleared with treatment, although the skin lesions reappeared after penicillin was discontinued. The 1 patient who had tuberculosis and bronchiectasis had blood-streaked sputum for two days in the first week of treatment, expectorated about 15 cc of blood twelve days after penicillin was initiated and also had blood-streaked sputum for several days during the third week of treatment, he had, however, had similar symptoms before — severe hemoptysis on two occasions one year previously, with streaking over a period of three or four weeks. There has not been a sufficiently long follow-up period to determine the duration of the symptomatic benefits. It was noted, however, that cough and expectoration again increased but that the general well-being continued after cessation of therapy.

In 7 patients, there was a change in physical signs, with the chest appearing clearer, owing to a decrease in the amount of moisture. The white-cell counts and sedimentation rates revealed no significant changes during treatment, except in 1 case, in which a marked diminution in leukocytosis occurred.

The assay studies revealed the following results. With intramuscular penicillin (Case 3), only once was the drug found in the sputum. This was on the first full day of treatment, and the assay showed 0.4 units per cubic centimeter. That there was good systemic absorption was indicated by blood levels of 0.2, 0.3 and 0.4 units per cubic centimeter and the presence of considerable penicillin in the urine. The lack of penicillin in the sputum of patients receiving intramuscular treatments was also found by White et al.<sup>7</sup>

The first patient treated intratracheally alone (Case 2) received 1,000,000 units in ten days. A very high penicillin titer was found in the sputum, with an average of 284 units per cubic centimeter, which assured an excellent topical or bronchial effect. The penicillin was given in a selective manner by instillation in the diseased lobes. That excellent pulmonary absorption occurred was indicated by the high blood and urine levels, with probable good parenchymal effect. The urine concentration averaged 38 units per cubic centimeter, which meant that over 30 per cent of the total dose given was recovered in the urine. The blood levels were 0.4, 0.5 and 0.6 units per cubic centimeter. Penicillin was recovered from the sputum for eight days and from the urine for three days after treatment was discontinued.

The next three intratracheally treated patients (Cases 4, 5, and 6) received 1,000,000 units in four days. Extremely high concentrations of penicillin were found in the sputums, with an average of 331, 552 and 159 units per cubic centimeter, respectively. The low level in the last patient was due to the fact that the administration of the drug was somewhat difficult and that not all of it reached the lung. The urine concentration averaged 38, 19 and 36 units per cubic centimeter, respectively. In 2 cases the blood level did not rise above 0.1 units per cubic centimeter, and in 1 case it reached 0.25 and 0.45 units. In these patients penicillin was found in the sputum for no longer than 3 days and in the urine for no longer than two days after treatment was stopped.

Although an extremely high sputum concentration of penicillin was obtained for a short time, this method of rapid intensive administration had several significant disadvantages. A penicillin concentration in the sputum beyond an optimum level, or one adequate to control the bronchial and parenchymal infection, is undesirable because the excess penicillin is lost in the expectoration. The amount of penicillin absorbed through the lung is indicated by the concentration in the urine and blood. The penicillin levels in the urine and blood of these 3 patients were lower than that found in the patient given the same dose over a period of ten days instead of four days. Penicillin was also found for a shorter time in these patients after the treatment was stopped. Because of this, it was decided to utilize the penicillin in the form of a smaller dose and to administer it over a longer period.

The next patient (Case 7) received 50,000 units intratracheally for thirty days, a total dosage of 1,500,000 units. The assay studies revealed an average sputum concentration of 101 units per cubic centimeter, a urine level of 8.3 units and a blood concentration of 0.1 to 0.25 units. These concentrations were less than those found in the patients given penicillin intratracheally for four to ten days. The results of treatment were not so

good as in the patient with ten days of therapy. The hoped-for benefit of prolongation of treatment for thirty days was apparently offset by the fact that the dosage was too small. Moreover, daily intratracheal instillations for more than a short period are definitely undesirable. It was therefore decided to use penicillin by inhalation, since this is an extremely simple method of administration. Our<sup>9</sup> previous experience with nebulization had indicated that drugs so given penetrate the lung, provide a topical effect and diffuse into the blood stream.

The first patient treated by inhalation (Case 8) received 1,500,000 units in thirty days (50,000 units daily). The penicillin concentration in the sputum was quite low and, although it varied greatly, averaged only 13 units per cubic centimeter — a lower concentration than that in any of the other patients except the one given intramuscular injections. The urine concentration, 1.8 units, was also the lowest in any patient. Assay of the blood showed no penicillin present on three occasions and 0.1 and 0.2 units per cubic centimeter at two other times. These low concentrations indicate that not all the penicillin vaporized enters the lungs. A certain portion reaches the buccal mucosa, pharynx and esophagus and is swallowed with the saliva. Yet with the concentration of penicillin noted in this case, a good clinical and bacteriologic effect was evident.

It was decided that a larger dose was needed to build up a higher concentration in the bronchi and that the administration should be continued for a longer period of time. The next patient treated by inhalation (Case 9) received 4,000,000 units in sixty days. The penicillin concentration in the sputum varied greatly but was maintained at a fairly high average level (86 units per cubic centimeter). This proved that inhalation in proper dosage could result in a favorable topical effect in the bronchi. The urine concentration averaged only 2 units per cubic centimeter, however, and three blood specimens failed to reveal any penicillin. These figures when compared with those in the intratracheal injection cases show that with inhalation there was much less bronchial and pulmonary absorption of penicillin. No assay studies were done in the last 3 patients treated at St. Clare's Hospital.

Two patients have had no follow-up, and 3 are still being treated. Of the other 7 patients, 2 were seen a month after treatment was stopped, 1 was followed for three months, 2 were followed for three and a half to four months, and 2 were followed for six and a half months.

## DISCUSSION

Boyd<sup>10</sup> in describing bronchiectasis states

There is a combination of inflammation and degradation of tissue. The wall of the bronchus is congested and

infiltrated with chronic inflammatory cells. The mucous membrane is atrophic and the epithelium may be completely absent in places. In advanced cases, various elements of the bronchial wall, the glands, the muscle and the elastic tissue may have more or less disappeared and be replaced by dense fibrous tissue.

Hinshaw and Schmidt<sup>11</sup> write

If one reviews the pathologic picture of true bronchiectasis one sees how difficult it is for nature to repair such damage. There has been extensive destruction of irreplaceable structures in the walls of important bronchi with resultant functional impairment of the air channels and accumulation and putrefaction of secretion which lead to further destruction and greater functional impairment.

The destructive changes of bronchiectasis are irreversible but the findings in the present series point to possibilities for the control of bronchiectasis. This study has shown that extremely favorable results can be achieved in the treatment of bronchiectasis with penicillin. Although the sputum was not entirely eliminated, a great diminution in expectoration occurred. It was demonstrated that the extremely foul sputum odor could be removed, organisms practically eliminated, and purulence greatly reduced. Intratracheal penicillin produced the latter two effects within a few days, and inhalation produced them in one or a few weeks. Symptomatic improvement, invariably of considerable degree, also took place. When treatment was discontinued, expectoration increased, organisms reappeared, pus cells became more numerous, and in many cases the odor returned. The sputum level was below the original one, and much of the symptomatic improvement persisted. These findings indicate that the results of treatment can be properly judged only after a long follow-up period and not by immediate changes alone.

It is generally accepted that the only cure for bronchiectasis is lung resection. Most, if not all, of the patients in this series, however, could not be treated surgically because of multilobar and bilateral involvement, and instead received palliative or symptomatic treatment. Moreover, all but the last 3 patients had only a short temporary course of treatment.

We wish to emphasize that while the penicillin was administered and for some time thereafter, excellent results were obtained, which represent a definite accomplishment in the treatment of bronchiectasis. A method has been demonstrated that can also be used in the preoperative preparation of patients for lung resection. With the expectoration markedly diminished and the sputum free of organisms, it is believed that the bronchiectatic lung can be handled during operation with little danger of aspiration into healthy pulmonary tissue and with diminished chances of an empyema should a bronchial fistula occur.

If the subjective and objective improvements obtained by our patients while on penicillin can be indefinitely continued by prolongation of treatment, a form of therapy is available in nonsurgical cases with marked advantages not present in other

nonoperative methods. This therapy requires the use of penicillin for an extremely long period, and perhaps indefinitely, somewhat in the manner that insulin must be constantly taken to control diabetes. The last 3 patients in this series are still being treated after intervals as long as sixteen weeks, and the penicillin will be continued. Because of the sustained effectiveness of continued therapy, although no cure may occur, it seems likely that the progressive and irreversible progress of the condition to chronic invalidism and death can be interrupted. Possibly the occurrence of pulmonary complications — bronchitis, pneumonia, lung abscesses and empyema — and the general consequences of bronchiectasis — amyloidosis, cardiac failure and brain abscesses — can also be reduced or prevented. The control of the bronchiectatic condition is of particular value during the winter months when pulmonary complications are rife. It is also possible under this treatment to remove the "psychic, social, economic and physical handicaps" of bronchiectasis.

Heretofore no therapy has been available that could control the bronchial and pulmonary infection of bronchiectasis. Penicillin has definitely curtailed the evidences of suppuration in our cases. It is within the range of possibility that penicillin in sufficient dosage and administered for a long enough period may eliminate the bacterial infection and abolish the expectoration and that repair may ensue. Although this program may be utopian, our findings indicate that the further use of penicillin is well justified.

Studies are now under way to determine the precise dose and length of treatment that will achieve the best results. Intramuscular injection therapy is not being employed because of the negligible amount of penicillin obtained in the bronchial secretions and the discomfort of repeated injections. The intratracheal route gives the most effective local concentration of the drug combined with a high absorption rate. For the treatment of bronchiectasis, penicillin is required over a long period, and it is not advisable to have daily intratracheal instillations or intrabronchial catheterizations for so long a time. There are the difficulty of anesthesia, the presence of sensitivity to cocaine and the possibility of reaction from manipulation with a bronchial catheter, as occurred in Case 7. A short intensive course with intratracheal instillations of at least 100,000 units daily is, however, suggested as suitable for preoperative preparation for lung resection because of bronchiectasis. This method can also provide an immediate maximum and rapid effect prior to continuation of penicillin by inhalation, as was done in Cases 10 and 11. Repeated short courses may also be of value.

Penicillin inhalation is effective, and when given in proper dosage provides an excellent bronchial concentration and parenchymal absorption. The inhalation method is, moreover, the simplest pro-

edure of any available. There is somewhat of a loss in its administration, however, and not all the drug reaches the lungs. For a result comparable to that achieved with intratracheal instillation, much more penicillin has to be used, but the increasing availability of the drug and its lowered cost warrant the use of this method. Inhalation is not necessarily a hospital procedure and is easily applied either in the physician's office, the clinic or the patient's home. The vaporizer is extremely easy to employ with an oxygen tank or by hand, although the latter method is the more difficult of the two. Experience has shown that patients can easily be taught to utilize a vaporizer and oxygen tank at home, and this has been done in the treatment of chronic pulmonary emphysema.<sup>12</sup> Penicillin can be used in this manner over a long period of time, since there are no evidences of toxicity.

It is desirable to treat adequately the sinusitis that is often present in patients with bronchiectasis. This reduces the possibility of drainage of purulent material from the sinuses to the respiratory tract.

In using the treatment described on a long-term basis, one must also take into consideration the possibility that the organisms will in time show resistance to the penicillin. In 3 of our cases, a few organisms reappeared during treatment. Treatment over a much longer period is required to gain definite information on this point. Gallardo<sup>13</sup> studied 112 cases of traumatic wounds of the extremities and draining abscesses and determined the naturally resistant and fast strains of staphylococci, both pathogenic and nonpathogenic. Nine and four tenths per cent of these organisms acquired resistance to the penicillin, and 12.4 per cent had natural resistance. The exact period at which the organisms became fast was not known, but differences of five to forty days were noted. Gallardo considers it advisable to assay routinely the sensitivity of bacteria from infected foci in all patients in whom penicillin is contemplated or in progress. Demerec<sup>14</sup> studied the production of strains of staphylococcus resistant to various concentrations of penicillin, and found that such strains could be obtained by growing the bacteria on mediums containing increasingly higher concentrations of the drug. Resistance was not induced or acquired through interaction between the bacteria and the penicillin, but appeared as an inherited characteristic that originated through mutation. The development of penicillin-resistant staphylococci during therapy has been attributed to the use of sublethal concentrations of the drug and is considered of little clinical significance.<sup>15</sup>

This question of resistance of organisms is still an unsettled one and its relationship to therapy is yet to be determined.

## SUMMARY

A report is made of 12 cases of severe bronchiectasis treated with penicillin.

The drug was administered by intramuscular injection, intratracheal injection and inhalation and combinations of these.

The total dosage of penicillin varied from 550,000 to over 5,500,000 units, and the length of treatment from four to one hundred and fifteen days. In 3 cases, therapy is still being continued.

The concentration of penicillin in the sputum was highest with intratracheal administration, less with inhalation and lowest with intramuscular injection.

The most rapid results were achieved with intratracheal instillations.

The simplest method of administration is inhalation.

Remarkable results were achieved with treatment. The sputum was considerably diminished and its odor was removed, most organisms were eliminated, and purulence was reduced. Considerable symptomatic improvement also took place. These changes were maintained while the penicillin was continued but did not long persist when it was stopped.

As symptomatic therapy for nonoperative cases and possibly for the control of bronchiectasis, penicillin will be required over a long period of time and perhaps indefinitely.

Penicillin given intratracheally and by inhalation is also suggested as a form of preoperative preparation for lung resection for bronchiectasis.

The results justify the further investigation of the use of penicillin in the treatment of bronchiectasis.

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A low-pitched, rumbling, mid-diastolic murmur appeared at the mitral area in a number of patients. It usually developed after two to three months of hospitalization, but was observed as early as three weeks after admission, raising the question of a pre-existing mitral lesion, notwithstanding the patient's denial of antecedent rheumatic infection. This murmur was best elicited during forced expiration with the patient lying in the left oblique position. In 5 cases, — none with aortic insufficiency, — it was transitory and disappeared within four weeks.

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The spleen was slightly enlarged in 5 cases.

Skin lesions, when present, were usually those of erythema multiforme, but in some cases small ecchymotic areas were noted at the site of the affected joints, spreading to involve the other parts of the extremities. Subcutaneous nodules were not found in any patient of this series.

Rapid loss of weight, amounting to as much as 16 to 20 pounds, was almost invariably noted during the acute stage of the illness.

Electrocardiographic changes were observed in 63 per cent of the patients, often after only a few days of illness. These occurred with increasing frequency when serial electrocardiographic studies were made. The most frequent abnormality was prolongation of the auriculoventricular conduction time, the longest PR interval being 0.62 second. In a number of cases, although the PR intervals were within the range of normal (0.12 to 0.21 second), repeated electrocardiograms showed variations in excess of 0.02 second. These variations were inter-

preted as being significant of first-degree auriculoventricular block. They emphasize the importance of frequent electrocardiographic tracings in the same patient. All degrees of auriculoventricular block were observed, and occasionally that of the indeterminate type was seen. At times the QRS complexes were inverted and notched in Lead CF<sub>4</sub>, and the ST segments were either elevated or depressed beyond normal in one or more leads. The T waves often became tiny, diphasic or inverted in one or more leads, especially in Lead CF<sub>4</sub>. In the patients with physical signs of pericarditis, the T waves usually became inverted in the limb leads but the ST changes were slight. Premature systoles were frequently noted. Of the other arrhythmias, paroxysmal auricular tachycardia, auricular fibrillation and auricular flutter occurred in isolated cases. The occurrence of interference dissociation in 18 cases was of clinical interest, although of no pathological significance. This abnormality, ascribed to hyperirritability of the auriculoventricular node, occurred only during the acute stage of illness. The electrocardiographic changes were transient in almost all the cases, usually returning to normal within seven to twenty-one days but occasionally persisting for as long as five months. When right or left ventricular preponderance developed, it generally remained during the entire period of observation. It is noteworthy that the electrocardiographic abnormalities were more frequent and also more marked in the patients admitted to the hospital during the peak of the epidemic periods.

An increased sedimentation rate has generally been regarded as a constant finding in acute rheumatic fever. In the vast majority of cases our findings were in agreement with this observation, but in a small number of patients with mild joint involvement and electrocardiographic evidence of first-degree auriculoventricular block the sedimentation rate was repeatedly normal. Thus, the deduction may be drawn that a normal rate does not preclude the existence of active rheumatic fever.

The white-cell count usually showed a leukocytosis, ranging between 10,500 and 16,000. In the minority of patients, a mild hypochromic anemia was found. Albuminuria, pyuria and microscopic hematuria were frequently present on admission, they generally disappeared within several days.

#### COURSE

The course was variable, depending on the tenacity of the rheumatic infection. The great majority of patients recovered after a single bout of fever and ran a relatively benign course. In the others, either the acute stage was followed by a long period of low-grade activity or the remission was punctuated by a recrudescence of symptoms, usually subsequent to a hemolytic streptococcus infection of the upper respiratory tract. It is well recognized that the danger of disabling heart disease

## THE CLINICAL ASPECTS OF RHEUMATIC FEVER IN ADULTS\*

COMMANDER DAVID H. ROSENBERG (MC), USNR†

**R**HEUMATIC fever has been generally regarded as a disease principally affecting children, and its occurrence in adults has as a consequence been more or less ignored. The high incidence of this disease among members of the armed forces has, however, served to focus attention on its importance in older persons, particularly young adults. It is the purpose of this paper to present a composite picture of the clinical aspects of rheumatic fever as observed in a series of 1000 patients studied at a large naval hospital.

## ETIOLOGY

Although the etiology of rheumatic fever remains unknown, epidemiologic studies indicate that there is a close relation between the disease and epidemics of Group A beta-hemolytic streptococcus infections. In almost all our patients, there was a recent history of an acute upper respiratory infection, such as coryza, sinusitis, pharyngitis, tonsillitis or otitis media, which occurred one to four weeks prior to the onset of rheumatic fever. In some cases, scarlet fever ushered in an attack of rheumatic fever. In 6 patients, acute polyarthritis and carditis appeared during the course of German measles, but whether these manifestations were due to the virus of that disease or were related to a previous unrecognized hemolytic streptococcus infection cannot be stated with certainty.

Exercise, fatigue and damp, rainy or cold weather were found to be provocative factors. As in many other acute infectious diseases, there was a distinct seasonal variation, with the highest admission rate from December to April, inclusive, when the disease reached epidemic proportions.

Contrary to expectations, in only 38 per cent of the patients was it possible to elicit an antecedent history of rheumatic fever, chorea, growing pains or heart trouble. In many cases there was a familial history of rheumatic fever suggesting a constitutional factor.

## INCIDENCE

The ages ranged from seventeen to forty-one years, with most patients between seventeen and twenty-four. All but 5 patients were men, which may to a large measure be explained by the relatively small number of women on duty in the district from which these patients originated.

## SYMPTOMS AND FINDINGS

The clinical manifestations were extremely varied. In most cases, the onset was marked by the appearance of acute arthritis, with pain, swelling, stiffness,

tenderness and often redness of one or more joints. The knees, ankles, wrists, elbows and small joints of the feet were those most frequently affected, although no joints escaped involvement. These symptoms were accompanied by malaise, lassitude, fatigue, tachycardia and fever ranging from 99 to 104°F, and were followed by similar involvement of other joints. Often the initial joint involvement persisted and the other joints successively became affected. The knee joints often became greatly distended with synovial fluid. Epistaxis was not infrequent, but drenching sweats were observed only rarely.

In many patients the clinical picture was less typical than the foregoing one, and it was occasionally bizarre. In some cases only mild pain and stiffness involving a single joint were noted, tachycardia, systemic manifestations and objective findings being absent. In many such cases, when the knees, ankle or foot were affected, the symptoms were misinterpreted as the result of a coincidental fall, sprain or even weak arches and were treated by immobilization. In other cases slight redness, mild tenderness and minimal swelling were encountered.

In one group of patients the only symptoms were vague muscular pains and stiffness. In another, chills and intermittent fever were the only complaints. Lumbar backache was frequent and was often accompanied by urinary frequency and the microscopic findings of pyelonephritis.

Of particular significance is the fact that the presenting symptoms were often abdominal, consisting of pain, with anorexia, nausea and vomiting and at times with diarrhea. Diffuse abdominal tenderness, with or without the rebound phenomenon, was usually found. In some of these cases the clinical picture simulated that of acute appendicitis, but a careful history and close observation revealed joint pain, tenderness and stiffness, followed by evidence of acute carditis.

In 15 cases, the principal symptoms were precordial pain and dyspnea, with or without cyanosis. In these cases the joint manifestations were minor and were generally disregarded by the patient. Various degrees of auriculoventricular block, sometimes extending to complete heart block with ventricular rates as low as 20 per minute, were found by electrocardiographic studies.

Cerebral manifestations, when present, were mild, consisting mainly of drowsiness and stupor. Rarely, transient psychoses with delirium were observed in the acutely ill patients with high fever. Choreia was present in only 3 patients. In 5 patients with stiffness and pain in the cervical vertebrae, meningitis was closely simulated.

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†Associate in medicine, Northwestern University Medical School, and adjunct attending physician, Michael Reese Hospital, Chicago (on leave of absence).



A perceptible increase in the size of the heart was observed in only a small number of patients while they were under observation. In most of these cases the enlargement was slight, unless complicated by acute pericarditis with effusion. Frequently, however, the first sound at the mitral area became muffled or diminished in intensity. In most cases a soft, blowing systolic murmur developed at the mitral area. In many of these patients it became audible over the entire precordium, and in some it became loud and harsh and was transmitted to the axilla. The systolic murmurs varied in intensity and degree of transmission from time to time and often disappeared when the patient was in the sitting position.

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Electrocardiographic changes were observed in 63 per cent of the patients, often after only a few days of illness. These occurred with increasing frequency when serial electrocardiographic studies were made. The most frequent abnormality was prolongation of the auriculoventricular conduction time, the longest PR interval being 0.62 second. In a number of cases, although the PR intervals were within the range of normal (0.12 to 0.21 second), repeated electrocardiograms showed variations in excess of 0.02 second. These variations were inter-

preted as being significant of first-degree auriculoventricular block. They emphasize the importance of frequent electrocardiographic tracings in the same patient. All degrees of auriculoventricular block were observed, and occasionally that of the indeterminate type was seen. At times the QRS complexes were inverted and notched in Lead CF<sub>4</sub>, and the ST segments were either elevated or depressed beyond normal in one or more leads. The T waves often became tiny, diphasic or inverted in one or more leads, especially in Lead CF<sub>4</sub>. In the patients with physical signs of pericarditis, the T waves usually became inverted in the limb leads but the ST changes were slight. Premature systoles were frequently noted. Of the other arrhythmias, paroxysmal auricular tachycardia, auricular fibrillation and auricular flutter occurred in isolated cases. The occurrence of interference dissociation in 18 cases was of clinical interest, although of no pathological significance. This abnormality, ascribed to hyperirritability of the auriculoventricular node, occurred only during the acute stage of illness. The electrocardiographic changes were transient in almost all the cases, usually returning to normal within seven to twenty-one days but occasionally persisting for as long as five months. When right or left ventricular preponderance developed, it generally remained during the entire period of observation. It is noteworthy that the electrocardiographic abnormalities were more frequent and also more marked in the patients admitted to the hospital during the peak of the epidemic periods.

An increased sedimentation rate has generally been regarded as a constant finding in acute rheumatic fever. In the vast majority of cases our findings were in agreement with this observation, but in a small number of patients with mild joint involvement and electrocardiographic evidence of first-degree auriculoventricular block the sedimentation rate was repeatedly normal. Thus, the deduction may be drawn that a normal rate does not preclude the existence of active rheumatic fever.

The white-cell count usually showed a leukocytosis, ranging between 10,500 and 16,000. In the minority of patients, a mild hypochromic anemia was found. Albuminuria, pyuria and microscopic hematuria were frequently present on admission, they generally disappeared within several days.

#### COURSE

The course was variable, depending on the tenacity of the rheumatic infection. The great majority of patients recovered after a single bout of fever and ran a relatively benign course. In the others, either the acute stage was followed by a long period of low-grade activity or the remission was punctuated by a recrudescence of symptoms, usually subsequent to a hemolytic streptococcus infection of the upper respiratory tract. It is well recognized that the danger of disabling heart disease



lies principally in the cases that pursue one or the other of the latter courses. In this series, the paranasal sinuses were found to be the usual focus of persistent infection, the eradication of which shortened the course of the disease.

Only 5 fatalities occurred. In 3 of these cases, there was evidence of terminal uremia and autopsy revealed subacute glomerulonephritis. In the other 2, death resulted from congestive heart failure.

### DIAGNOSIS

In the typical case, when acute migratory polyarthritis is found in association with acute carditis, electrocardiographic abnormalities, leukocytosis and an increased sedimentation rate, the diagnosis of rheumatic fever may be made without equivocation. As indicated by the foregoing description, however, many patients do not present this combination of findings, and in these the diagnosis is likely to be difficult and the clinical picture confusing. Indeed, the manifestations of rheumatic fever may be so similar as to simulate those of many diseases. Hence, in patients with fever accompanied by arthralgia, muscular pains and stiffness, precordial pain and dyspnea, acute abdominal symptoms or acute pyelonephritis and in whom the diagnosis is in doubt, as well as in those with pyrexia of unknown origin, the possibility of rheumatic fever must receive consideration. It is unfortunate that there exists today no specific diagnostic test for rheumatic fever, and until such a test is forthcoming, careful and prolonged clinical observation is necessary in these cases. Errors in diagnosis may be inescapable, especially in patients with arthralgia and low-grade fever, representing the milder forms of rheumatic fever, a fact that has also been emphasized by Jones.<sup>1</sup> A history of antecedent rheumatic fever or chorea should be regarded as highly significant, whereas a familial history of rheumatic fever may be of some help and should receive consideration. Electrocardiographic changes, particularly prolongation of the conduction time, should be considered as strong evidence in support of rheumatic fever, but it must be recognized that they are not diagnostic and that at times other infections produce similar changes (Rosenberg<sup>2</sup>). The development of systolic murmurs per se cannot be regarded as of diagnostic value, inasmuch as they may appear during the course of any acute infectious disease and are usually produced by relative dilatation of the cardiac orifice, but the appearance of diastolic murmurs at the left third interspace near the sternum or at the aortic area, mid-diastolic murmurs at the mitral area — in the absence of aortic regurgitation — or signs of acute pericarditis may be considered as confirmatory. Determination of the antistreptolysin titer may be helpful, but only as an indication of a recent hemolytic streptococcus infection. In doubtful cases the absence of anti-

streptolysins tends to negate the diagnosis of rheumatic fever.

Of the many diseases that may resemble rheumatic fever, acute rheumatoid arthritis is the most frequent one. It may be differentiated by the persistent periarticular swelling of the small joints, resulting in deformities, a predilection for the proximal interphalangeal joints of the fingers and the usual freedom from cardiac involvement. It should be pointed out, however, that the relation between these diseases is still controversial and that they may coexist. Gonococcal arthritis may confuse the diagnosis, but the recovery of the specific organism from the joint fluid is conclusive evidence. The finding of gonococci in the genitourinary tract in a patient with a recent history of gonorrhea may also be regarded as presumptive evidence of gonococcal arthritis. On the other hand, a positive complement fixation test has not by itself been found to be a reliable diagnostic aid. Septic arthritis and arthritis secondary to other acute infectious diseases may be suspected from the antecedent history of infection or from the concomitant disease. Undulant fever is generally associated with arthritis and may be identified by the finding of a high titer of specific agglutinins in the blood serum, by intradermal skin tests or by positive blood cultures. Serum sickness may also produce febrile reactions with acute polyarticular manifestations. On the other hand, a history of serum administration seven to ten days previously, the presence of urticaria and the absence of redness of the joints serve to differentiate the disease. The premeningeal stage of acute meningococcemia, when accompanied by acute arthritis, may resemble acute rheumatic fever. It may be distinguished by the history, the presence of a generalized petechial eruption and corroboratory bacteriologic studies. Acute gout at times masquerades as rheumatic fever. In these cases, the hyperuricemia, roentgenographic findings in the bones and a prompt response to colchicin leave little doubt as to the correct diagnosis. Other diseases, such as disseminated lupus erythematosus and periarthritis nodosa, may require differentiation, but they are far less frequent than those just discussed.

### TREATMENT

The treatment of these patients consisted of complete bed rest and the giving of 2500 to 3000 cc of fluids daily, 8 to 10 gm of sodium salicylate and 6 to 8 gm of sodium bicarbonate daily, 0.033 gm of codeine sulfate when indicated for severe joint pain and a high-calorie, high-vitamin diet. Salicylism occurred with extreme infrequency with the lower dosage. Patients with gastric distress received 4 gm of sodium salicylate in 120 cc of starch solution as a retention enema four times daily. In some cases 0.67 gm of amidopyrine or 1 gm of acetylsalicylic acid, administered four times daily instead of enemas, was well tolerated. When amidopyrine was

administered, the white-cell count was followed closely

These dosages were usually maintained for two weeks. When the patient became asymptomatic, and the sedimentation rate normal, the dosage was reduced by a half and continued for another month. In the event of a relapse when the influence of the drug had worn off, whether with or without fever, salicylates and bed rest were resumed and were continued until the sedimentation rate had remained normal for two or more weeks. The efficacy of salicylates in the suppression of such recurrences was clearly demonstrated in these cases.

All patients were kept at complete bed rest for a minimum period of six weeks, and it was required that the temperature, pulse, sedimentation rate and white-cell count were normal before the patient was permitted out of bed. Depending on the degree of cardiac damage, bed rest was generally maintained for four to six weeks after the electrocardiogram had become normal. The period spent out of bed was slowly increased and physical activities were graduated, special attention being devoted to the pulse.

Under such management, the joint involvement, fever and tachycardia usually subsided within three or four days, and the sedimentation rate generally returned to normal in two or three weeks. In the acutely ill patients, improvement was more protracted, seven to fourteen days elapsing before the joints, temperature and pulse became normal. With continued improvement the heart sounds returned to normal, and gallop rhythm, when present, disappeared. Systolic murmurs frequently diminished in intensity or became confined to the mitral area, in many cases they disappeared, even though formerly loud and widely transmitted.

Coburn's<sup>3</sup> therapeutic technic was employed in some of the acutely ill patients and in those who were refractory or showed gastric intolerance to oral therapy. Doses of 1000 to 2000 cc of 1 per cent sodium salicylate in isotonic saline solution were administered daily by slow intravenous drip, a blood-salicylate level of at least 350 microgm per cubic centimeter being maintained. This regime was continued until the patient was asymptomatic and afebrile, and until the sedimentation rate had dropped by about 20 per cent. When these criteria were fulfilled, intravenous treatment was replaced by oral therapy. Relief of symptoms was often effected more rapidly by this method than by others, and patients refractory to oral therapy were at times benefited. Nausea, vomiting, tinnitus and deafness, however, occurred quite often, and in 2 cases marked cerebral symptoms were noted in the form of delirium and stupor, which disappeared when salicylates were discontinued.

Sulfadiazine was given to 5 patients according to the plan generally followed in the treatment of pneumonia. No beneficial effects were noted, on

the contrary, the polyarthritis became intensified and the fever remained high and continuous. No conclusion could be drawn concerning any untoward cardiac effects. In all cases, the symptoms subsided promptly when salicylates were substituted.

Penicillin was administered to 5 patients in doses of 20,000 units intramuscularly every three hours to a total of 1,000,000 units. Electrocardiograms, white-cell counts and sedimentation rates were taken daily, and the patients were kept under close observation. No beneficial effects could be attributed to this form of therapy, nor were any ill effects noted. These conclusions are in agreement with those reported by Watson, Rothbard and Swift<sup>4</sup> and by Foster, McEachern et al.<sup>5</sup> A prompt symptomatic response was obtained with salicylates in these patients.

Digitalis was employed only in patients with congestive heart failure or a persistent tachycardia of 125 or more and in those with auricular fibrillation and flutter. Aspiration of the pericardial sac was not found necessary in any patient with pericardial effusion. In 2 patients with extensive pleural effusion, thoracentesis was required for the relief of marked respiratory embarrassment.

Residual stiffness and mild aching in the joints were noted in some patients after all evidence of active rheumatic infection had disappeared, these were especially prominent during cold or damp weather. Diathermy and massage were beneficial in many of these cases. The mild aching in the feet and ankles observed on walking was improved by whirlpool baths.

Finally, although the maintenance of a high nutritional state is important, it is agreed that to attain the ultimate goal in the recovery of patients with rheumatic fever all efforts must be directed to the prevention of recurrences. Recent studies conducted by Thomas and her co-workers,<sup>7</sup> Coburn<sup>8</sup> and Holbrook<sup>9</sup> suggest that the incidence of recurrences may be significantly reduced by the elimination of hemolytic streptococcus infections through the prophylactic use of sulfonamide drugs. Additional well controlled studies will be necessary, however, to settle this matter beyond doubt. Furthermore, in drawing conclusions from such studies one must not lose sight of the probability that resistant strains of hemolytic streptococci may be encountered in some localities and in different epidemics. In such cases, sulfonamides are ineffective.

#### SUMMARY

A composite picture of the clinical manifestations of acute rheumatic fever as observed in a series of 1000 patients in the naval service is presented.

The importance of recognizing rheumatic fever in adults is emphasized, and the difficulties in its early diagnosis are discussed.

The therapeutic effects of salicylates, sulfadiazine and penicillin are recorded.

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## AINHUM\*

MAURAY TYE, M D †

BOSTON

**A**INHUM, or spontaneous dactylolysis, which occurs predominately in male Negroes, has been described as a distinct disease by some authors and as a symptom by others. At the digitoplantar fold there appears a constricting ring of fibrous tissue, which deepens and finally strangulates the underlying structures, producing spontaneous amputation.

Weinstein<sup>1</sup> gives Messum<sup>2</sup> credit for the original description of the condition in 1821, but most authors give it to Clark,<sup>3</sup> who in 1860 described a lesion considered as a sequela to yaws in natives of the Gold Coast. The name of the disease and the first adequate description of it were published by da Silva Lima<sup>4</sup> in 1867, and the first pathological study was made by Wucherer.<sup>5</sup> Hornaday<sup>6</sup> in 1881 reported the first case in the United States, which occurred in North Carolina in a ten-year-old Negress.

According to Matas,<sup>7</sup> "ainhum" is derived from the Brazilian Negro *patois*, meaning "fissure." Da Silva Lima<sup>4</sup> traced it to the Nagos word meaning "sawing off." In one of the African dialects "ainhum" signifies "compression."

The greatest number of cases have been reported among the Negroes of the west coast of Africa, the West Indies and South America. Isolated cases have been reported from Europe, Russia, Istanbul and India, and about 45 cases have been seen in the United States—most of them in the southern states, a few in New York and the rest in localities scattered over the country. The case reported below is the first in New England.

A 77-year-old, unemployed Negro, a native of Barbados, West Indies, who had lived in and about Boston for the last 50 years, entered the hospital because of constriction and discoloration of the left 5th toe. He had been aware of this condition for 6 to 8 months before admission, but it had caused no symptomatic difficulty except a progressive gradual narrowing at the base. There was no history of trauma, no unusual footwear had been worn, and there had been no infection of the feet. The patient denied having had any venereal disease, by name and symptoms, diabetes or intermittent

claudication. No other members of the family had had a similar condition. The diet was adequate.

Physical examination on admission revealed a well developed, well nourished, well preserved Negro, able to walk without pain or discomfort. The temperature was 98.8°F., the pulse 90, the respirations 20, and the blood pressure 170/100. The patient was mentally alert and intelligent. The skin was not discolored and was of good texture, and



FIGURE 1

there were no keloid changes. The left 5th toe was purplish, warm, supple and slightly larger than the corresponding right toe. It was fissured at the digital plantar fold. Its distal portion, which was adherent at the lateral margin of the foot, was held only by a fibrous band 0.5 cm in diameter. There was no discoloration of any of the other toes. The pulsation of the dorsalis pedis artery was faintly palpable. Sensory and vibratory sensations were physiologic, and there were no abnormal reflexes.

The hemoglobin was 90 per cent and the white-cell count 5500, with 60 per cent neutrophils, 22 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils. The red cells appeared normal. The serum nonprotein nitrogen was 35 mg

\*From the Department of Dermatology and Syphilology, Boston City Hospital.

†Graduate assistant in dermatology and syphilology, Boston City Hospital, teaching fellow in dermatology and syphilology, Boston University School of Medicine.

per 100 cc., and the fasting blood sugar 95 mg. A blood Hinton test was negative. The urine was yellow and had a specific gravity of 1.020. It contained no albumin, sugar or bile. The sediment showed 1 or 2 white cells per high-power field, but no red cells or casts.

X-ray examination showed absence of the middle phalanx of the little toe and destruction of the proximal portion of the terminal phalanx, with marked osteoporosis (Fig 1). The distal and middle portions of the proximal phalanx of the 5th toe were absent, only the base and a small, markedly narrowed fragment of the shaft remaining. There was atrophy of the bones of the foot, most marked in the toes.

There was a sharp constriction in the soft tissues of the 5th toe, which was almost completely separated from the foot. In a few days the toe became cold, dry, shriveled, firm and black and hung loosely, held only by a narrow tag of sclerotic tissue (Fig 2).

The fibrous band was cut with scissors and the toe was painlessly removed. There was neither bleeding nor ulceration, and only a small fibrous tab of tissue remained. There was no discoloration of the skin proximal to the site of amputation. The patient remained completely asymptomatic and was discharged. Follow-up in the Out-Patient Department 2 months later showed no change in the condition of the foot.

Microscopical examination of the epidermis showed the stratum corneum to be thickened, most markedly so near the point of amputation, the stratum lucidum was not identified but the stratum granulosum was clearly defined. Nuclei were preserved in this and deeper layers. Pigment remained in the basal cell layer. The derma was composed of dense connective

tissue, hypertrophy of the epidermis and pressure on vasomotor nerves, resulting in the trophic phenomena. A theory that the condition is a result of leprosy, advanced by Pacha,<sup>9</sup> has been discarded as a result of histologic studies and bacteriologic examinations that have never shown the leprosy bacillus. Similarly, the belief that syphilis is a causal factor has been discarded. Scheube,<sup>10</sup> Weinstein<sup>1</sup> and Abbe<sup>11</sup> advanced the concept of ainhum as a trophoneurosis, but no nerve lesions have been found. Some writers, notably Wellman,<sup>12</sup> have considered infection by chiggers an etiologic factor. Davies and Hewer<sup>13</sup> suggested that chronic epidermophytosis might produce an excess of scar tissue and thus constriction of the toe. Constrictions resembling those of ainhum have been described in scleroderma<sup>14</sup> and in keratoderma.<sup>15, 16</sup> Bloom and Newman<sup>17</sup> considered the pathologic process as a mechanical one produced by a fibrotic constriction induced by some previous mechanical or infectious injury.

A few cases of this disease have been reported in white persons, notably by Arby, Debrum, Hyde-Montgomery and Castellani, according to Bloom and Newman.<sup>17</sup> Weinstein<sup>1</sup> and Doyle<sup>18</sup> believed that there was some familial tendency toward the disease. Ainhum rarely attacks those who have not reached adolescence, the greatest incidence being in persons between twenty and forty years of age. Weinstein,<sup>1</sup> however, stated that following the literature he was struck by the comparative old age of some of the patients. About 10 per cent of the cases in the United States have developed in persons between sixty and eighty years old.

Ainhum usually affects one or both of the fifth toes at the first interphalangeal articulation, either simultaneously or successively—rarely the fourth toe and less frequently the second phalanx. It generally begins as a circular depression at the internal, inferior aspect of the web of the little toe and gradually progresses, surrounding the toe, with the outer margin the last part to be involved. In most cases there is no pain at the commencement of the disease, but late in the course this symptom may be prominent. The portion of the toe distal to the locus of constriction frequently swells to a large globular segment with an intact nail. Later the phalangeal bone at the level of the constriction divides, the skin color changes, and there is loss of voluntary control. All this requires from six months to several years to develop, the course in most cases covering two to five years.

Spinzig<sup>19</sup> summarizes the pathological findings as follows:

A hypertrophy of the epidermis occurs in the vicinity of the constriction. The papillae are elongated and enlarged. The arteries are thickened and engorged with blood cells, while the veins are usually empty. There is some perivascular infiltration of round cells. In the corium are usually arranged bundles of connective tissue with fat and some round-cell tissue and edema. The sweat



FIGURE 2

tive tissue. Within the derma and the dermal papillae, as well as within the deeper subcutaneous tissues, there were large numbers of dilated, thin-walled vessels, which were largest and most numerous just distal to the point of amputation. There was a decrease in the amount of remaining bone, which consisted of irregular trabeculae. Fat filled the trabecular spaces. No bone was found just distal to the point of amputation, where collagenous connective tissue had replaced the bone. Strands of collagenous connective tissue surrounded the centrally placed bony trabeculae. In longitudinal sections nearest the point of amputation, the tissue was composed of skin and a central core of collagenous connective tissue.

Many theories have been advanced to explain this condition. Da Silva Lima<sup>4</sup> has suggested that injuries to the toes by sharp grasses produce contracting cicatrices, but the disease has been reported in Negroes who have worn shoes, and it does not occur equally in all races accustomed to going barefoot. Eyles<sup>8</sup> believed that the digitoplantar fold was a favorable site for irritation from foreign

glands show signs of atrophy. A rarefying osteitis involves the bone with areas of destruction. Those areas are filled with connective tissue and fat and the bone is gradually replaced with fibrous tissue.

X-ray examination demonstrates the soft-tissue constrictions, there is complete or partial bony absorption of the distal phalanx and the proximal phalanx, although still present usually shows some absorption of the distal portion.

Many entities are to be considered in the differential diagnosis, but most of these are readily excluded. Leprosy mutilans is ruled out, according to Acton,<sup>20</sup> by the presence of anesthesia of the part, as a result of which trauma and burns produce ulcers that extend to the joints. Furthermore, all the toes are usually involved in this disease.

Morvan's disease and syringomyelia are excluded by the fact that in these diseases sensory disturbances of cold, heat and pain are lost, together with muscular power. The arms are generally affected as well.

Another condition to be considered is scleroderma. In this disease the skin is indurated, multiple digits are affected, and constitutional symptoms are frequent. The incidence is highest among females. The indurated, localized bandlike counterworkings may, however, offer difficulty in differentiation.

Congenital constrictions of the digits are usually not limited to the toes and are generally present from birth.

Castellani<sup>21</sup> believed amputation to be the best method of treatment. Da Silva Lima<sup>4</sup> thought that if the constriction was cut perpendicularly early it might be cured, but according to Gerwig and Warner,<sup>22</sup> splitting of the fibrous band is often followed by recurrence. Irgang and Alexander<sup>23</sup> relieved the pain in 1 case with sodium iodide. Others have tried calcium, thyroid and parathyroid, without success. Lumbar sympathectomy<sup>24</sup> and plexus treat-

ment, with alternation of positive and negative pressure, have failed to influence the disease.

## SUMMARY

The first case from New England of ainhum, or spontaneous dactylolysis, is reported. The results of pathological study and the roentgenologic findings are reported, and the literature is reviewed.

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## SYMPOSIUM ON MEDICAL SOCIOLOGY

## FOREIGN PROGRAMS OF MEDICAL CARE AND THEIR LESSONS\*

FRANZ GOLDMANN, M D †

IT IS a simple matter to state that complete medical care of the finest type is wanted for the greatest possible number of people at the least possible expense, but it is a Herculean task to translate such a need into a practical and workable plan. In the course of some sixty years, various types of medical-care programs have been tried out in a score of foreign countries. There is a wealth of experience regarding the relative merits of the basic methods of organizing and administering programs for the care of the sick. Some of the fundamental principles introduced late in the nineteenth century have proved to be sound and capable of wide application, others have been found to be inadequate, although they have not fallen into complete oblivion. In concern for tomorrow one must not forget the lessons of yesterday — and there are many lessons to be learned from both the achievements and the shortcomings of policies for organizing medical care.

Instead of describing details of some of the programs adopted abroad, I shall focus attention on the common elements in the vast number of developments that have taken place when enthusiasm crystallized into programs, and on the guiding principles of organization and administration that have emerged in the process of a piecemeal, and often haphazard, growth. I shall briefly discuss the methods of organizing professional services and facilities for medical care, the methods of organizing payment for medical care, the administrative organization of medical-care programs and the social philosophy underlying foreign developments.

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In organizing professional services, the prevailing policy has been, and still is, to preserve the old-established principles of practicing medicine — those of private practice, individual practice and free choice of a physician. In a score of countries these three principles have been incorporated in social-insurance laws as well as in public-assistance statutes. They have been observed regardless of the method chosen for organization of payment for professional services. As experience accumulated, the wisdom of continuing the old policy was increasingly questioned. There was little inclination

to discard the principle of private practice, but there have been some exceptions to the rule that deserve mention.

Russia, in line with her political ideology, has chosen the system of salaried medical service under government control. Private practice, although not forbidden, plays no role worth speaking of. Some hundred rural "municipalities" in certain Canadian provinces, notably Saskatchewan and Manitoba, have adopted the so-called "municipal doctor scheme," under which one or several salaried physicians are employed by the community to render service to all residents. A few months ago the Saskatchewan Government announced plans for the extension of this system throughout the province. Similar programs have been introduced in some rural areas of Australia, in particular in the Northern Territory, Queensland and Tasmania.

Whereas the principle of private practice has been maintained in the vast majority of all foreign countries, the system of individual practice has been increasingly criticized. There has been growing realization of the need to adjust medical practice to the rapid scientific progress and the profound socioeconomic changes that have taken place since the nineteenth century — the good old days when there was justification for the saying, "God cures the sick and the doctor takes the fees." It is now generally recognized that the attainment of quality, efficiency and economy of service is of prime importance in planning for the future. Two specific problems stand out as particularly pressing: the co-ordination of the work of the general practitioner and the specialist, since the latter should complement rather than supplant the former, and the integration of so-called "preventive" services and "curative" services, since these cannot be separated without injuring both.

To improve the situation, the introduction of the group practice of medicine has been increasingly recommended, primarily in the last two decades. The term "group practice" denotes a system of co-operative practice of medicine by physicians for the purpose of pooling experience and skill, facilities and equipment, technical and other auxiliary personnel and operating expenses, if not also earnings. Group practice is first of all a method to promote the scientific co-operation of the medical and allied professions for the welfare of the sick. Although it has no direct relation to the method of paying for medical care, the system gains in value if the economies it affords are passed on to the patient.

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†Associate clinical professor of public health, Yale University School of Medicine, New Haven, Connecticut.

Well organized group practice conducted from a properly staffed and well equipped center, such as a clinic or a hospital, greatly benefits the patient, the health professions and the community. It provides for better and more service in a convenient way, serves to attain consistency and continuity of treatment and reduces the costs of medical care for both patients and physicians. It gives the physicians and related groups opportunities for professional improvement through consultation, research and postgraduate study, a satisfactory income, greater freedom from night calls, Sunday work and evening hours, and paid vacations. It fills a gap in the community-health program by making good medical care, both preventive and curative, available at reasonable costs.

On a limited scale, group practice has been developed in a few countries, such as Chile, France, Germany and Peru, in all instances in connection with social-insurance programs. It is interesting that in Germany group practice was abolished by the Hitler régime in line with its political ideology. Even the limited experience gained abroad clearly shows that group practice compares favorably with individual practice, since better and more service can be given at lower costs, and this tallies with the experience acquired by group clinics in this country. Significantly, recent legislative proposals in Canada and Great Britain recognize group practice and want to try it out on a larger scale. Going a step farther, the National Health and Medical Research Council of Australia has proposed the general introduction of group practice, along with the establishment of a system of so-called "consultation centers" throughout the country.

The lesson that can be learned from the development abroad is as follows. Originally, little attention was paid to the organization of professional services, and major emphasis was placed on the development of payment plans based on the insurance principle. Belatedly, it was recognized that failure to adjust the organization of professional services to modern requirements endangered the effective and economical operation of any organized program of medical care.

The organization of hospitals and clinics abroad has advanced remarkably far. The major problem was to decide on the responsibility for construction and equipment and the improvement of all the medical-care facilities necessary to meet individual requirements as well as to satisfy the community's need for adequate, humane and economical service. There are two schools of thought abroad. One group believes that all medical-care facilities ought to be established at public expense, exactly as is done with schools, highways, utilities, recreational facilities and similar services essential for the welfare of the individual as well as that of the social organism. Opponents of this policy — and there are many — insist that public policy should not deny

scope and opportunity in one of the most appealing fields to the expression and practice of freely accorded individual benevolence. They do not, however, question the obligation of government to provide for certain types of facilities.

Actually one finds four distinct policies abroad. In Russia, all hospitals and clinics are owned and operated by the state. In a considerable number of countries, the great majority of all hospitals and clinics are built by local, state or national governments. Nongovernmental activities in this field are not only permitted but closely co-ordinated with those of public agencies. Nongovernmental facilities, however, must meet strict requirements as to quality, have a license to operate, and accept supervision by public authorities. Another group of countries believe that government's responsibility should be confined to provision of selected types of facilities, such as isolation, mental and tuberculosis hospitals and certain types of preventive clinics, voluntary organizations being encouraged to provide for general and allied hospitals as well as clinics of various types. Still another group of countries, including some in South America, have encouraged the construction of hospitals by social-insurance organizations.

A few examples will serve to illustrate some of these policies. In Sweden and Great Britain, all isolation hospitals are government-owned. Great Britain has about 1000 public isolation hospitals with some 40,000 beds. In Sweden, Great Britain and New Zealand, nearly all beds for mental patients are in governmental institutions, as compared with 97 per cent of such beds in this country. In Great Britain, about three fourths of all the tuberculosis beds are in public institutions, as compared with more than four fifths in the United States. In the Scandinavian countries, Austria and Germany, general hospitals are mainly public, and nongovernmental hospitals are utilized and paid by public and semipublic agencies for services rendered to designated groups. A predominantly voluntary system of general hospitals is found in France and Great Britain, although lately voluntary facilities have been losing ground. Clinics under public auspices constitute the vast majority of such facilities in a large number of countries, including the Scandinavian countries, Great Britain, Ireland, Austria, Germany and several South American countries. In Great Britain, more than 2000 school clinics and about 2500 maternal and child-health centers, or four fifths of all these centers, are maintained by public authorities.

In a score of countries, the marked change in social philosophy, expressed in the shift from private to public responsibility for the establishment of all necessary medical-care facilities, has raised intricate problems. Some groups and individuals argue that there is no longer any justification for the voluntary hospital system and hold that nongovernmental

ospitals should be abolished in favor of a system of public hospitals. Others believe that voluntary hospitals should not be prevented from operating, provided that they meet standards of adequacy and are functionally co-ordinated with governmental hospitals. The clinic problem too is being hotly debated. In the course of a haphazard development numerous types of clinics have come into existence, some organized for preventive service only, some emphasizing treatment service, some serving exclusively the needy and some admitting selected groups of self-supporting patients. The wisdom of continuing such artificial distinctions is increasingly questioned, and a new approach to the clinic problem is urged. Instead of a variety of clinics with different functions and serving different socioeconomic groups, there should be established medical centers or health centers to provide both preventive health services and care in sickness for all residents of the community. These centers should serve as the headquarters of physicians and related groups in private practice as well as of personnel employed by public and private agencies. Pertinent recommendations to this effect appear in several legislative proposals recently advanced in foreign countries.

\* \* \*

There are two basic methods of organizing payment for professional and institutional services: taxation and insurance. When the method of taxation is used, revenues are raised primarily through taxes on property and income and to some extent through excise taxes such as sales, liquor and tobacco taxes. When the method of insurance is employed, the funds are raised in a quite different way. Insurance against the economic hazards of sickness, injury and maternity is a method of pooling risks and resources to budget and pay the cost of medical care or to compensate for loss of earnings due to disability, or to fulfill both these functions. The principle of insurance implies that many persons must band together under a single plan to spread their risks and must make small regular prepayments into a common fund to pool their resources. Thus, health insurance is organized self-help to remove or reduce the financial burden that may arise from sickness, injury or maternity. People can budget and pay for services and cash benefits when they are well and earning; they can obtain service to prevent illness and incapacity for work and receive medical care and compensation for disability when they are sick and disabled.

Both methods of financing medical care are in wide use abroad, although there are significant differences in the extent to which they are employed. Russia, in 1937, abandoned the method of financing medical care through insurance and since that time has been supporting her medical-care program out of general tax revenues. Only a few services, such as convalescent care and treatment

in health resorts, are still financed through social insurance. In many other foreign countries the method of taxation is employed on a more limited scale. The policies differ greatly from country to country owing to wide variations in needs and available resources as well as in social philosophy. A few examples will serve to illustrate this point.

In Sweden, tax funds defray all but about 15 per cent of the expenditures for operating communicable-disease hospitals. This is an outstanding example of a policy designed to support the control of communicable disease by providing for most liberal hospitalization at public expense without regard to the economic conditions of the patient. In Ireland, there are a large number of public treatment clinics, and the policy responsible for them dates back to the early nineteenth century. These centers provide for home care as well as clinic care and serve all persons in need; the interpretation of such need is quite liberal. In a large number of countries, such as Austria, Germany, Great Britain and the Scandinavian countries, the tuberculosis-control or venereal-disease-control program, or both of them, are supported primarily out of tax funds. The eligibility standards for medical care at public expense are such as to enable the large majority of the people to receive any service they need. In some countries, there developed a multitude of special tax-supported programs with different standards of eligibility and service, all operating separately. That such a policy inevitably has patchwork results is now fully recognized. An attempt has been made in recent proposals to remedy the situation by integrating special programs into over-all programs. Nearly all foreign countries use tax funds to pay for the medical care of selected groups of persons, primarily war veterans and the recipients of public assistance. Extension of tax-supported medical care to self-supporting persons is widely regarded as unsound policy. The system of public medical care for those in need necessarily involves application of the person involved and determination of his eligibility by a so-called "means test." Under this system, the applicant and his family must have exhausted most, if not all, of their own resources before they can be accepted for a service that in the final analysis is a last resort. Charity, well intended as it is, is not what the common man wants. Restriction of service to persons in need jeopardizes preventive action. It comes too late to prevent complications, serious illness and chronic stages of sickness, and too late to permit the most economical use of the taxpayers' money. It is the considered opinion of nearly all experts abroad that the public-assistance approach to the organization of medical care is highly undesirable, and that it should be employed as little as possible.

Recognizing the inadequacy of the public-assistance approach to health security, a steadily



persons able to make regular prepayments, and it is hard to establish and to administer in thinly settled areas. For these reasons, all the countries having compulsory sickness-insurance programs also maintain complementary programs of medical care financed out of general tax revenues

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The administrative organization of foreign programs of medical care is distinguished by a well known feature: multiplicity of agencies. A few significant trends may be discussed briefly. Usually, the national governments have accepted responsibility for nationwide policy-making and, to varying extents, for supervision of standards and financial participation. They share responsibility with governments at other levels. Small administrative units have been more and more discarded, since they have proved inadequate for the purpose of financing and administering medical-care programs. Instead, large units, such as counties, districts and regions, are vested with financial and administrative powers and functions. Administration of compulsory sickness-insurance schemes is generally separated from the administration of all other health services and entrusted to special statutory bodies. Thus, a state within the state has been created. The result has been overlapping, friction and waste of administrative effort on the one hand and neglect of some fields of health service on the other. The old principle of lay control of health services has been more and more abandoned in favor of professional supervision of professional matters — the physician, the dentist, the pharmacist and others each being responsible in his own field. These professional persons have authority to decide on the technical and professional aspects of medical care under social-insurance as well as other programs

\* \* \*

Planning for adequate medical care is more than a method of organizing the application of scientific

knowledge and technical skill. It is the expression of a social philosophy. It is effective only in so far as it is sustained by a conviction of principle. The philosophy underlying modern health policy abroad rests on two cornerstones — society's need of the fit and productive person and the individual's right to health.

In essence, these ideas were expressed as far back as the end of the eighteenth century, when France issued the Declaration of the Rights of Man, and again in recent national constitutions, such as those of the Weimar Republic and the Union of Soviet Socialist Republics. New concepts have emerged, holding that the health of the people is a public concern, that sickness is more than a private misfortune, and that medical care in its widest sense is an essential human right, to be guaranteed and safeguarded in any program for personal and social security. Protection of the right to health is a fundamental function of any society aspiring to a genuine and rational economy of human resources and values. Government of the people, by the people and for the people has an obligation in this field. Nobody has expressed this better than Abraham Lincoln: "The legitimate object of government is to do for a community of people whatever they need to have done but cannot do at all, or cannot do so well for themselves, in their separate and individual capacities."

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32051

#### PRESENTATION OF CASE

A fifty-six-year-old janitor entered the hospital complaining of weakness.

Seven weeks before admission he consulted a physician because he did not feel well. He was told that he was anemic and was given liver injections. Ten days before admission he felt dizzy and faint, and at about the same time his skin became somewhat yellow. The urine was not dark, nor were the stools clay colored. At no time had the patient complained of nausea, vomiting, diarrhea or constipation. He had lost 25 pounds in weight in six months, despite a good appetite.

Physical examination revealed a pale, thin man in no acute discomfort. The skin and scleras were slightly yellow. The heart and lungs were normal. The liver edge was palpated 7 cm below the right costal margin, it was smooth and slightly tender. The prostate was smooth, firm and symmetrically enlarged.

The temperature was 99°F, the pulse 80, and the respirations 20. The blood pressure was 100 systolic, 60 diastolic.

The red-cell count was 2,100,000, with 49 gm of hemoglobin. The white-cell count was 12,000, with 82 per cent neutrophils. Many macrocytes were present, but the red cells were generally normochromic. The mean corpuscular volume was 85 cu microns, the mean corpuscular hemoglobin 20.8 micromicrogm, and the mean corpuscular hemoglobin concentration 24.4 per cent. The urine was normal. The nonprotein nitrogen was 19 mg per 100 cc. The total serum protein was 5.9 gm per 100 cc, with 3.0 gm of albumin and 2.9 gm of globulin. The serum calcium was 7.7 mg per 100 cc, the phosphorus 1.5 mg, and the alkaline phosphatase 27.5 Bodansky units. The serum bilirubin was 0.9 mg per 100 cc direct, and 1.3 mg indirect. The serum cholesterol was 156 mg per 100 cc. A cephalin flocculation test was ++ in twenty-four hours, and ++++ in forty-eight hours. The prothrombin time was 21 seconds (normal, 15 to 17 seconds). A bromsulfalein test showed 20 per cent retention. The gastric juice contained free hydrochloric acid. The stools varied

from yellow to gray, and five out of seventeen specimens were guaiac positive.

An x-ray film of the chest was essentially negative. A gastrointestinal series revealed a normal esophagus. A small portion of the fundus of the stomach protruded through a hiatus hernia but was easily reduced. The second part of the duodenum was constantly rigid in its upper portion, with an irregular filling defect and loss of mucosal pattern along its medial wall, which contained a small central ulceration (Figs 1 and 2). A questionable defect was present in the lower portion of the ascending part of the duodenal loop, where the mucosal

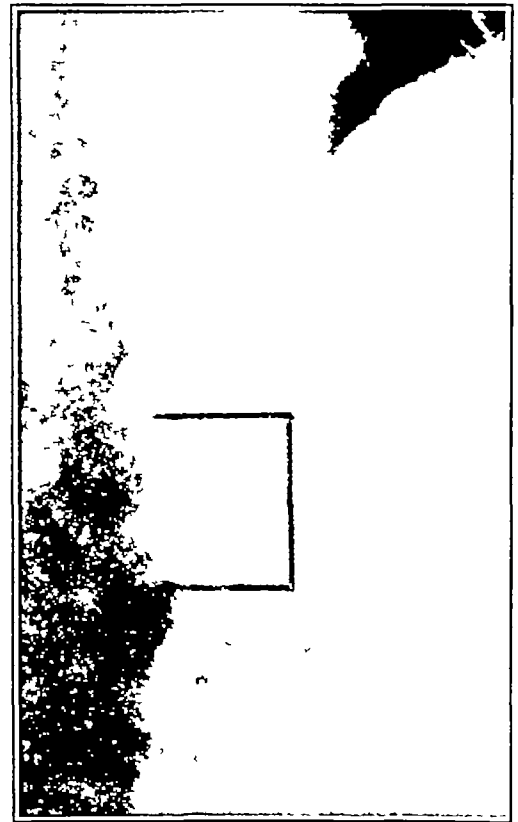


FIGURE 1 Roentgenogram Showing Narrowed and Rigid Area of Second Portion of Duodenum

pattern was preserved. A barium enema was negative.

An operation was performed.

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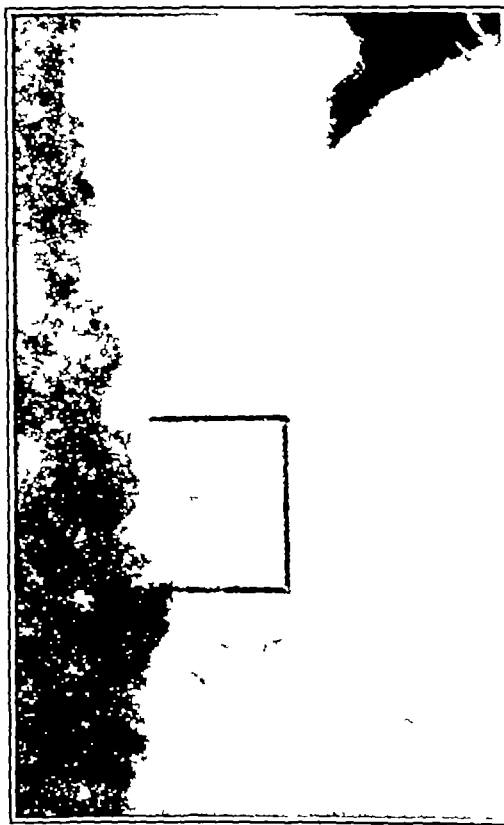


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little fleck that looks like barium in a punched-out defect. This shadow corresponds to the position of the ampulla of Vater.

DR BARTLETT: Where is the other defect that was mentioned in the ascending portion?

DR SCHULZ: It must have been a fluoroscopic observation or recorded on a film that we do not have here.

DR BARTLETT: This man of fifty-six had been sick for seven weeks, at any rate that is when he first went to his doctor. We do not know how much longer he had had symptoms. He had been losing weight for six months but had had no symptoms referable to the gastrointestinal tract.

Physical examination adds that he was slightly jaundiced and had a palpable liver, which extended well below the costal margin. Quite a good deal of



FIGURE 2 Enlarged View of Region of Ampulla of Vater Showing Punched-Out Defect (arrows)

laboratory work was done — much of it because of the macrocytes seen in the smear, I presume. The various studies on the blood cells afford evidence pointing to a secondary rather than a primary anemia, although that statement is subject to correction by someone who knows more about hematology than I do. The serum bilirubin was slightly elevated, corresponding with the slight clinical jaundice. The various studies referable to the liver seem to indicate some impairment of liver function.

Certainly in a man like this we should look sharply for a malignant neoplasm somewhere. Since we are told that this man had lost 25 pounds and that his jaundice was increasing, we have to assume that it was an obstructive type of jaundice and must look for the source of the obstruction. He had had no pain, and with bleeding into the gastrointestinal tract, as shown by a positive guaiac test on repeated occasions, and a blood picture like this,

one would strongly suspect a malignant tumor. I believe that we can rule out gallstones. We have x-ray evidence that suggests a lesion in or adjacent to the duodenum that had ulcerated through into the duodenum. So as I see it, my function is to make a choice between a lesion of the ampulla or in the duodenum proper and a lesion in the head of the pancreas that had ulcerated into the duodenal wall. I do not know any way to make a sure decision. Since Dr Schulz has suggested that the lesion was in the region of the ampulla, I will put that as my first choice, with carcinoma of the head of the pancreas as the second.

DR TRACY B MALLORY: You are assuming that, if the lesion was in the ampulla, it was malignant?

DR BARTLETT: Yes.

DR JAMES H TOWNSEND: Was no attempt made to visualize the gall bladder?

DR MALLORY: A peritoneoscopy was done preoperatively. It showed a smooth, enlarged, bile-stained liver and a slightly dilated gall bladder. No fluid was found in the abdominal cavity, and a liver biopsy showed only bile stasis.

#### CLINICAL DIAGNOSIS

Carcinoma of head of pancreas

DR BARTLETT'S DIAGNOSIS

Carcinoma of ampulla of Vater

#### ANATOMICAL DIAGNOSIS

Adenocarcinoma of ampulla of Vater.

#### PATHOLOGICAL DISCUSSION

DR MALLORY: Dr Scannell, I believe that you operated on this man. What were your findings?

DR JOHN G SCANNELL: This man was operated on in two stages. The first consisted of drainage of the gall bladder and the establishment of a feeding jejunostomy. At that time a mass was palpated in the head of the pancreas, but its size could not be accurately determined. In two weeks we re-explored, and a small freely movable tumor was demonstrated in the head of the pancreas in the region of the ampulla; this mass was fairly readily resected. The common duct, I might add, which was not well visualized at the first exploration, was found to be tremendously dilated; the gall bladder was dilated, but the edema had completely disappeared.

DR MALLORY: At the second operation, considerable portions of the duodenum and head of the pancreas were resected. The tumor appeared to be limited to the ampulla. It involved the full thickness of the duodenal wall, but so far as we could make out it did not penetrate the pancreas. There were no obvious lymph nodes. The area of resection appeared to be entirely adequate. I do not believe that the prognosis is excellent, but it is not impossible that a cure has been effected.

DR BARTLETT: What type of tumor was it?

DR MALLORY An adenocarcinoma, fairly well differentiated. It is worth remembering in considering operation on such a patient that benign polyps of the ampulla are not extremely rare. Exploration, at least, is certainly indicated.

DR BARTLETT Was the duodenum ulcerated?

DR MALLORY There was slight ulceration of the surface of the tumor. No gross crater was evident.

DR BARTLETT What was done with the bile duct? Was the surgery complicated?

DR LELAND S MCKITTRICK I like the way that Dr Scannell passed over that.

DR SCANNELL A loop of jejunum was selected about 45 cm below the ligament of Treitz, it was transected, and the proximal end was implanted into the side of the distal portion. An end-to-end anastomosis was then effected, after the manner of Dr Allen,\* between the cut ends of the common bile duct and the distal jejunum over a catheter, which was led out through the wall of the jejunum and through the abdominal wall, to be removed in about three weeks. The cut ends of the pancreas and of the stomach were then implanted into the side of this loop.

DR MALLORY Did the patient develop a pancreatic fistula?

DR SCANNELL On the tenth postoperative day he drained considerable material from the upper end of the wound, but this has since decreased to nil. From the character of the material I should judge that it was from a high jejunal or pancreatic fistula. We were unable to demonstrate the pancreatic duct at the time of exploration and therefore implanted the cut end of the pancreas into the subserosa of the jejunum.

## CASE 32052

### PRESENTATION OF CASE

A sixty-five-year-old woman entered the hospital complaining of abdominal pain.

For two years before admission she had had an intermittent dull ache in the right upper quadrant. The pain occasionally radiated to the back and was not associated with nausea, vomiting or anorexia. It had no relation to the ingestion of food. It lasted for about twenty-four hours, subsided and then recurred in a few days. At times she also had dull aching pain across the lower abdomen, not related to the distress in the right upper quadrant. The latter complaint was made worse by constipation but was not relieved by a bowel movement. An intermittent midepigastric distress had also been present for a year and a half. Five months before admission she was seen at another hospital, where she was told that she had a growth in the stomach. She was given a chalky milklike fluid, which she

took for three months and which seemed to relieve the epigastric pain and belching.

She had had rheumatic fever at twenty-five years of age, with no residual heart disease but with persistent joint pains. She had been known to have hypertension for fifteen years before admission and had been treated for syphilis for ten years, although she denied a history of venereal disease. Three years before admission she suddenly lost vision in the right eye, but it slowly returned. She had had three miscarriages.

The physical examination revealed a well developed and nourished woman in no acute discomfort. The pupils reacted normally to light and accommodation. The border of the heart was 11 cm to the left of the midline in the fifth interspace. A systolic murmur was heard over the aortic area. The lungs and abdomen were negative. Neurologic examination was negative.

The temperature was 97°F, the pulse 70, and the respirations 15. The blood pressure was 230 systolic, 110 diastolic.

The red-cell count was 4,200,000, with 12 gm of hemoglobin. The urine was normal. The non-protein nitrogen was 15 mg per 100 cc, and the total protein 5.9 gm. The chloride was 90 milliequiv per liter. A blood Hinton test was positive. Lumbar puncture yielded a clear fluid, with normal dynamics, the fluid contained 350 red cells per cubic millimeter. The total protein was 34 mg per 100 cc, and the gold-sol curve 0001100000.

A gastrointestinal series showed a normal esophagus and a small hiatus hernia. There was some narrowing, as well as absent peristalsis, of the prepyloric region of the stomach (Fig 1). No peristaltic waves were seen to pass through the immediate prepyloric region. It was not possible to palpate this area. There was an apparent crater about 8 mm in diameter somewhat toward the margin of the lesser curvature. The duodenal cap was small but not deformed. A barium enema showed numerous diverticula in the sigmoid. On gastroscopy the instrument passed readily. When first examined the angulus was tightly and smoothly closed, without any spasm or ropelike contraction. With air inflation the angulus opened and presented a normal appearance. Slow peristaltic waves were seen to pass over the proximal antrum, which appeared somewhat granular but was otherwise normal. The distal antrum and the pylorus were not visible. The body of the stomach appeared normal throughout.

An operation was performed.

### DIFFERENTIAL DIAGNOSIS

DR DANIEL S ELLIS I should like to call attention to the fact that this woman's pain was not associated with nausea, vomiting or anorexia. The history does not state whether she had these symptoms at the time of admission, yet I am forced

\*Allen A W. Method of re-establishing continuity between bile ducts and gastrointestinal tracts. *Ann Surg* 121:412-424 1945.

to conclude from the chemical values given in the laboratory data that the patient had been vomiting I do not know how else to explain the low chloride and the high carbon dioxide in the absence of renal disease

I assume that the red cells in the spinal fluid were due to the trauma of the tap. We are not told the result of the spinal-fluid Wassermann test. Perhaps the test was not done. In the absence of

do not represent just a puckered and swollen stomach wall. Certainly, it is not a normal mucosal pattern.

DR ELLIS: Is that the only film of the gall bladder?

DR SCHULZ: No, but it is a representative one.

DR ELLIS: May we see a film of the chest?

DR SCHULZ: None are available.

DR ELLIS: We have, then, the story of a patient, sixty-five years of age, who we know had hypertension of some degree, with cardiac enlargement,

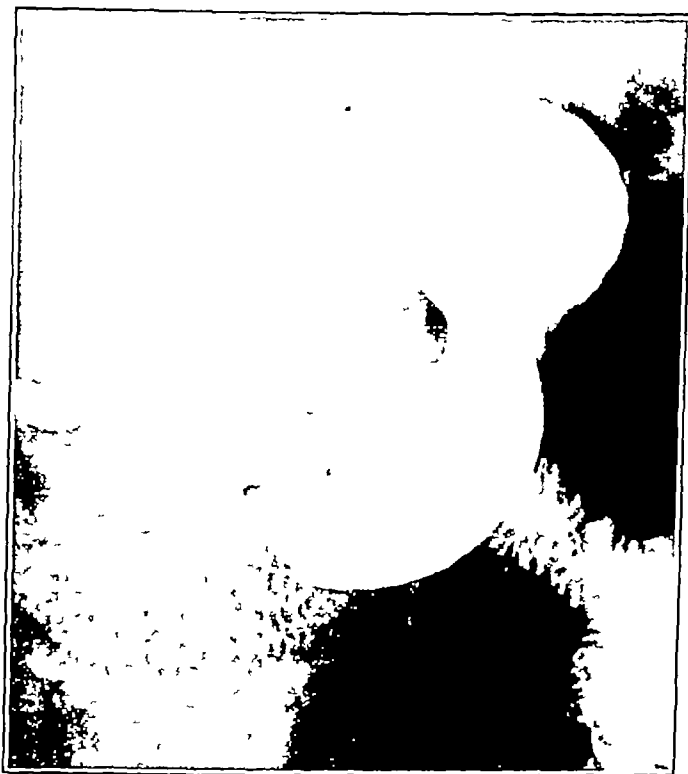


FIGURE 1 *Roentgenogram of Stomach following Barium Meal*

that information I am going to assume that the spinal fluid was normal.

From the available history there is one thing that I am sure of, namely, that an operation was a prerequisite of diagnosis.

May we see the x-ray films?

DR MILFORD D. SCHULZ: This film is put up simply to show that the colon and gall bladder were normal. This next film shows an area of irregularity in the antrum and in the prepyloric region of the stomach. This last film, I believe, shows best what was thought to have been an ulcer crater. There is apparently some rigidity about it along the lesser curvature side of the antrum and in the prepyloric region. The duodenal bulb is quite normal.

DR ELLIS: Can you see a mass in the prepyloric area?

DR SCHULZ: No.

DR ELLIS: What about the mucosal markings?

DR SCHULZ: They are not normal. Some markings look like mucosal folds, but I wonder if they

diverticulums of the sigmoid, which could account for the discomfort low in the abdomen, and a small hiatus hernia, which may or may not have contributed to her symptoms in the past. In addition, the factor of primary importance, — the one that apparently resulted in her hospitalization, — was a lesion of the stomach and, as I see it, my problem is to say what that lesion was.

It seems to me that the differential diagnosis is clear and lies between one of three things: carcinoma of the stomach, benign peptic ulcer and syphilis of the stomach. The latter diagnosis has rarely been proved. When it occurs it may resemble ulcer but is likelier to resemble carcinoma. It is usually associated with weight loss, vomiting, anorexia, anemia and achlorhydria. The criteria for a clinical diagnosis of gastric syphilis are the proper age group (usually under forty), collateral evidence of syphilis, x-ray evidence of a tubular prepyloric obstruction, improvement under anti-syphilitic therapy and a lesion found at operation with the microscopic characteristics of syphilis.

he symptoms and x-ray evidence, as well as the positive Hinton test, are the positive indications for such a diagnosis in this case. This patient, however, was in an older age group, and there is no evidence that ten years of antisyphilitic therapy had helped her stomach trouble.

On the basis of the patient's age and the location of the lesion the chances that this was a benign ulcer are remote. A benign ulcer, however, may have enough inflammatory reaction around it to give an x-ray picture such as the one we have just seen, and the fact that this patient was not anemic and was reported to be in a good state of nourishment also favors a diagnosis of a benign lesion, especially in the light of the prolonged history of symptoms and the proof of a gastric lesion of at least five months' duration.

Finally, we have to consider malignant disease of the stomach. This lesion is located in the prepyloric region, where 70 per cent of all gastric cancers are found. Twenty-five per cent of the remaining gastric tumors occur on the lesser curvature, and in this case there was an ulceration on the lesser curvature. To know whether this patient had achlorhydria and exactly how much weight she had lost would be helpful. As I said in the beginning, the one thing that I am sure of is that the only way an accurate diagnosis could have been made in this case was by operation, and even then, microscopic examination of the specimen may have been necessary.

In conclusion I shall say that I do not believe this woman had gastric syphilis or that she had a benign peptic ulcer. My final diagnosis is malignant disease of the stomach, probably an adenocarcinoma, with partial pyloric obstruction, she also had essential hypertension and hypertensive heart disease, diverticulums of the sigmoid, latent syphilis and a hiatus hernia, the last being an incidental finding and not contributing to her symptoms.

DR TRACY B MALLORY: Are there any comments or alternative diagnoses?

DR JAMES A HALSTED: Chronic gastritis might give this picture.

DR MALLORY: Has the roentgenologist anything to say about that?

DR SCHULZ: There is no evidence of fluid, and the gastric rugae are not greatly swollen.

DR MALLORY: Dr Scannell, will you tell us about the gross findings at operation?

DR JOHN G SCANNELL: We were intrigued by the prepyloric region at operation. The stomach was freely movable, with no gross retroperitoneal disease. There was an area of induration in the prepyloric area that involved the whole circumference of the stomach, not being limited to the lesser curvature. We thought it probably was benign disease, but we could not tell what it was. There were no enlarged lymph nodes, but since we were doing the operation for potentially malignant

disease, we removed the omentum and secured the left gastric artery at its source. On opening the resected portion of the stomach, we were still at a loss to explain the nature of the disease. There were shallow ulcerations in the mucosa, and the wall of the stomach was indurated but not adherent to surrounding structures.

DR FRANCIS M RACKEMANN: Was there any disturbance of the blood supply?

DR SCANNELL: No obvious disturbance.

#### CLINICAL DIAGNOSIS

Carcinoma of stomach

#### DR. ELLIS'S DIAGNOSIS

Carcinoma of stomach

#### ANATOMICAL DIAGNOSIS

Lymphoblastic lymphoma of stomach

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The pathologist was likewise unable to decide from examination of the gross specimen whether the lesion was benign or malignant, although the latter seemed a little more probable. The diagnosis had to wait for microscopic examination, which showed a malignant infiltrative tumor that proved to be a lymphoma and not a carcinoma.

Following resection, the patient was started on x-ray therapy, and she is still in the hospital undergoing treatment. The outlook in these cases is not too bad. With a combination of resection and radiation, "cures" of five or more years sometimes occur.

DR BENJAMIN CASTLEMAN: Were the lymph nodes involved?

DR MALLORY: No large nodes were found.

DR JAMES H TOWNSEND: Do lymphomas usually ulcerate?

DR MALLORY: They may or may not. Sometimes they produce extremely large ulcerations.

DR FLETCHER H COLBY: That means that a lymphoma may be localized?

DR MALLORY: In the gastrointestinal tract it is quite frequent to find localization in the wall of the viscus, with the immediate nodes entirely negative. Even when the nodes are enlarged there is frequently no microscopic evidence of infiltration.

DR SCHULZ: In the absence of involvement of the regional nodes or of remote disease, I wonder about the need for x-ray therapy with the lesion presumably so completely removed.

DR MALLORY: We have a few long cures on record from surgery alone, but there are not enough of these cases to compare with those receiving the combined treatment for statistical analysis.

DR FREDERICK KRAVES: What type of lymphoma was this?

DR MALLORY: We classified it as a lymphoblastic lymphoma, although the cells were not extremely immature.



# The New England Journal of Medicine

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The Journal does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## NATIONAL SOCIAL HYGIENE DAY

FEBRUARY 6 is National Social Hygiene Day, the tenth annual event of its kind on a national basis. It had its beginning as a series of meetings held across the country on the day of the annual meeting of the American Social Hygiene Association, being an alternate for members unable to travel to the meeting, but in 1937 it was given formal recognition by designating the day by this name. It has come to be a day on which pledges are renewed to the achievement of the high standards set by the founders of the Association. These founders had as their major objective the protection of the family and its members from the perils to health, happiness and home that result from venereal disease and prostitution. The full attainment of these aims is chiefly concerned with an attempt

to guide schoolteachers, religious leaders and parents, as well as physicians, in the furnishing of wise counsel concerning the sex problems of the younger generation. The achievement of its objective is a co-operative undertaking requiring the energies of local and national associations and groups of many types, such as health departments, social agencies, physicians, nurses, educators, church leaders and Army and Navy venereal-disease control centers, for its successful completion.

Great advances have been made in these ten years in the fields of diagnosis and treatment of syphilis and gonorrhea. The dramatic success of penicillin as a therapeutic agent is still unfolding, but the final estimate of its value, especially in syphilis, can only be measured by medical experience with the drug over a period of years. In the meantime the early diagnosis of syphilis and gonorrhea is essential. The campaign for the prevention of these diseases must proceed with increased vigor. Education, that is, education of the patient, the family and the public at large, is the essential feature of any preventive program directed at these diseases. The publication of a recent study by the Advisory Committee on Public Education for the Prevention of Venereal Disease of the United States Public Health Service\* occurred at an opportune moment. Among the recommendations of this committee three items should be emphasized: first, that venereal-disease education is a primary responsibility of official health agencies and should be conducted by them on an intensive and a sustained basis; second, that this education should be coordinated with other health-education programs; and third, that there should be a considerable expansion of facilities for training health-department personnel who are to engage in these activities.

Participation of the physician in this campaign for the protection of the individual and the family obviously demands early diagnosis, adequate treatment and the routine reporting of cases of venereal disease, as directed by the laws of his state. As a citizen as well as a physician he has a large obligation, by reason of his medical knowledge, to participate to the fullest extent in organized activities.

\*Report of United States Public Health Service Advisory Committee on Public Education for the Prevention of Venereal Diseases (July 15, 1945). *J. Fam. Dis. Inform.* 26:256-263, 1945.

the education of the public and the prevention these infections, in accordance with the plans developed by public-health departments and associations dedicated to this cause

### ELSE WHENCE THIS PLEASING HOPE"

MUCH has been written on the medical and surgical care of the patient, volumes have been published on the treatment of the mentally ill, but little has been said and even less has been written on the psychologic aspects of patients who are gravely ill or who are suffering from a fatal disease. An excellent approach to this subject has come from the pen of a layman, Ben Ames Williams,\* who, to his discomfiture but to the advantage of the public, has contrived from time to time to become ill. He has been able, therefore, "To see ourselves as others

see us" and to point out to us doctors the psychologic pitfalls that lie before us, but in addition he has given some very constructive and valuable advice concerning their avoidance. To those who have not read his article, we recommend it, to those who have, we suggest that they read it again.

In last week's issue of the *Journal* appeared the concluding paper of a series of articles on Hodgkin's disease, and therein are contained a few words of advice concerning the psychologic care of patients with a disease that is almost always but not invariably fatal. Of the last six words of the previous sentence the most important, far and away, are "but not invariably" for in these words lie one of the subtle secrets of the care of the patient.

What have we to offer to patients with this condition or allied ones? X-ray therapy, certainly, transfusions, probably, radical surgical intervention, rarely. Can we offer the hope of a true cure? Yes,

but only once in hundreds of cases. Yet, who can predict in the individual case, granting that it be early, whether or not a cure will result. Herein lies the second secret.

Above all we can offer hope. That we can and must give in order that the patient's days, whether they be short or long, be ever full of hope, not despair. Nearly three years ago a young soldier who had been through the Kasserine Pass both ways was suddenly invalided home for reasons quite

unknown to him, because he felt perfectly well. In the States he was with equal abruptness and greater bluntness told "the truth" — that he had leukemia, that he would live but a few months and that nothing could be done. Shortly after he was boarded out with a Certificate of Disability Discharge, he consulted a civilian doctor. From him he received hope, and the tense, distraught, despairing,

frightened soldier became a happy, hopeful young man. No diagnosis was mentioned. Rather it was stressed that much could and would be done and that he could reasonably look forward to an active and useful life. Indeed, his illness was so minimized that the patient came, quite surely, to believe that he did not have leukemia. Two years later he rather shyly slipped into his physician's hand a newspaper clipping about a new cure for leukemia. "I just thought I would ask if there is anything in that, doctor." "No, I'm afraid there isn't." No more was said. The boy had grown to know the truth, but its impact was gone because of the insidiousness of its realization. Today, three years and more after the battle of the Kasserine Pass, that boy is alive and happy and active. The diagnosis, if the real truth be known, is not entirely clear, but the facts are as stated. Hope we can give, the patient's burdens we can, to a great extent, take unto ourselves.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*  
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8 Fenway  
Boston 15, Massachusetts

\*Williams B. A. The Greeks had a word for it. *New Eng J Med* 233:427-432, 1945

But it is not always the patient who must be treated with gentleness it is not always the patient in whom we must, at all costs, inspire hope. He may be quite oblivious of the truth while his friends or relatives may be distracted almost beyond control. Then we must turn our attention to these good people, if only to protect the patient.

If we are to give hope we must learn the gentle art of evasion — not lying, mind you, but evasion. Recently an extremely astute man with some knowledge of medicine and indeed of his own disease, aplastic anemia, asked his physician point blank "Does it not follow, doctor, because my general health and sense of well being have greatly improved in the past two weeks and because the ulcerations in my mouth have entirely cleared, that my anemia will similarly improve?" It did not follow in the slightest. But cannot we reply without hesitation — to hesitate is to fail — that we hope that such will be the case and pass rapidly on to less contentious matters before the patient recognizes that we have said "hope" not "will"? That patient died ten days later at home, having in the meantime spent three days with friends in New York City. He had no wish to hurry home. Was he not filled with hope?

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MARCH 13. Worcester Memorial Hospital.

APRIL 10. Hahnemann Hospital.

MAY 8. Annual meeting.

# The New England Journal of Medicine

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Number 6

## SILENT AND MASQUERADING INTRATHORACIC LESIONS\*

### The Importance of Proper Identification of Lesions Discovered during X-Ray Surveys

RICHARD H. OVERHOLT, M.D.,† AND NORMAN J. WILSON, M.D.

BOSTON

MILLIONS of persons have recently had their chests x-rayed in the mass surveys of large segments of the population now under way. The program at induction centers and in the armed forces, industrial plants and schools is well known. In addition, some form of radiologic screening of the chest is becoming a routine procedure in many clinics and hospitals and in the private practice of many physicians. Thousands of pathologic lesions have been discovered in apparently healthy persons, a large percentage being in the minimal stage, when treatment offers the best chance of cure.

Of this group, the patient who presents one of the most difficult and important problems is the one with a lesion of the chest demonstrated by x-ray and associated with either no symptoms or those so mild that its seriousness and potentialities are unsuspected. These cases present a grave problem to the medical profession. Surveys find, but do not necessarily identify, disease. The proper identification and successful treatment of these early forms of intrathoracic disease demand serious attention.

There is evidence that the danger and the immediate threat of such lesions are too little appreciated. Waiting for time to tell the story is still prevalent. All too often the physician reassures his patient and asks him to return in a few months for a checkup, only to find at that time that a minimal tuberculous focus has developed into moderately advanced or far-advanced disease, or that a small tumor has either metastasized or extended so that it is no longer operable. Roentgenologists likewise frequently advise checkups in a few months in the face of disease processes that carry an immediate and dangerous threat. In the light of present diagnostic and therapeutic possibilities, time becomes a deadly enemy for many patients with intrathoracic lesions.

Recently Goorwitch<sup>1</sup> analyzed the effects of mass surveys in Los Angeles County, California, on the extent of pulmonary involvement in tuberculous males admitted to the Olive View Sanatorium. Although approximately two thirds of the lesions so found were minimal, no reduction occurred in the incidence of far-advanced disease among those entering the sanatorium. Goorwitch explained this by the fact that only a small percentage of those with minimal involvement were admitted. Such statistics leave unanswered the question of what has happened to the thousands of patients with minimal lesions uncovered in surveys and in private practice. To be sure, some of these are lost in the shuffle. Others refuse to enter a sanatorium for treatment. The histories of such cases, however, all too frequently point to the failure of physicians to appreciate the seriousness of the early lesion as the direct cause of the patient's delay in entering the sanatorium for proper treatment.

The same state of affairs exists with carcinoma of the lung. In 1942, Overholt<sup>2</sup> reviewed 153 such cases. Sixty per cent of these patients were not only incorrectly diagnosed by the first physician consulted but were treated on the basis of that diagnosis for long periods of time, an average of twelve months intervening between the onset of symptoms and the establishment of the proper diagnosis. In the average case the physician did not request an x-ray examination for three months after onset, and the correct diagnosis was not made for six months after the pulmonary lesion had been demonstrated by x-ray.

The foregoing facts establish the need for fundamental concepts concerning the diagnosis, evaluation and therapy of intrathoracic lesions. Naturally, the entire subject cannot be covered in a single paper of this kind, and only three outstanding types of condition uncovered in mass surveys will be considered — tuberculosis, carcinoma of the lung and mediastinal tumors.

\*From the New England Deaconess Hospital.

†Thoracic surgeon, New England Deaconess Hospital.

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physician not only at once to guard patients with innocuous lesions against long periods of unnecessary therapy, but — what is more important — to protect those with active lesions by giving prompt and energetic treatment

### *Evaluation of the Patient*

The evaluation of the patient who harbors the tuberculous focus is of prime importance. The age, sex, race and socioeconomic status are the chief factors to be considered.<sup>2</sup>

**Age** The evidence gained in mass surveys and in the study of serial x-ray films demonstrates that early tuberculous infiltration usually occurs between adolescence and the age of thirty. These lesions represent a focus of tuberculous bronchopneumonia, with a predominant tendency toward central caseation, excavation and bronchial spread. They constitute an immediate threat, and therapy must therefore be prompt and adequate. In the later decades of life, more of the chronic productive fibroid forms of tuberculosis are seen. Some of these patients require therapy because of residual or renewed activity. In others the lesion has been stable for many years and requires no therapy. In the latter type of case a period of watchful waiting is justifiable provided that complete studies have failed to show any signs of activity.

**Sex** It is also during the second and third decades that the factor of sex exerts its strongest influence. Tuberculosis in young women tends to be more active and fatal than in men of the same age group.

**Race** Although the influence of race is strongly disputed, there can be little doubt that under existing circumstances in most communities Negroes exhibit a lower resistance to tuberculosis than do Whites. This is evidenced by their greater tendency to develop acute pneumonic lesions and by their predisposition to dissemination of the infection through the lymphatics and blood stream.

**Socioeconomic factors** The patient's occupation and station in life also influence the prognosis. Clinical and epidemiologic studies show that poverty and debilitating working conditions are likely to be associated with progressive tuberculosis.

These factors are vital not only in evaluating the lesion but in prescribing treatment, because they render both steps possible on the basis of the underlying lesion. The clinical data must be interpreted pathologically if judgment is to be accurate and treatment adequate.

### *Study of the Sputum*

When a positive sputum has been found in a patient with a pulmonary infiltration, not only

has the diagnosis been confirmed but the need for active therapy has been established. Any lesion shedding tubercle bacilli harbors some activity. Nevertheless, it must be emphasized that a positive sputum is not a prerequisite for a diagnosis of pulmonary tuberculosis and that a negative sputum does not necessarily rule out activity. A positive sputum may never be demonstrated in inactive lesions and in many active ones of minimal extent. It has been repeatedly shown, however, that a sufficiently rigid study of the sputum will show it to be positive in the vast majority of active tuberculous lesions.

Two factors influence the accuracy of sputum examinations — the length of time over which the specimens have been collected and the method by which they have been examined. The examination of single specimens by the routine smear method is notoriously unreliable. In fact it is so inefficient that its use as a diagnostic procedure should be condemned. The use of a concentration technic increases positive findings by about 30 per cent. Pooled specimens the sputum having been collected from two to seven days further increase positive results. Multiple cultures and guinea-pig inoculations of pooled specimens should always be employed before one concludes that the sputum is negative. In the event that sputum cannot be produced, a study of gastric washings usually reveals the presence of tubercle bacilli if the pulmonary process is active. Secretions from the lungs that are carried to the upper air passages by ciliary motion of the mucosa and by gravity are swallowed during sleep so that the gastric specimen should be taken in the morning and before breakfast. Acid-fast organisms that are not tubercle bacilli are frequently found in the gastric specimen. For this reason, they should be identified by culture and guinea-pig inoculation.

Pinner and Werner<sup>4</sup> state that over 99 per cent of patients with active tuberculosis are found to have tubercle bacilli in secretions from the lungs if all methods of examination are utilized. Thus, when these tests are repeatedly negative in a patient with a progressive pulmonary infiltration the lesion is probably nontuberculous and other diagnostic procedures are indicated. For example, we have proved the presence of primary cancer in a considerable number of sputum-negative patients who had been treated for months for tuberculosis by bed rest and even pneumothorax.

### *Leukocytic Index and Erythrocyte Sedimentation Rate*

An altered leukocytic index or an elevated erythrocyte sedimentation rate usually indicates activity of the tuberculous lesion. Here again, however it must be emphasized that an active, progressive tuberculous focus may produce too little systemic reaction to cause any abnormality in either of these findings. In fact the vast majority

## TUBERCULOSIS

The evaluation of tuberculous lesions of small or moderate extent that are either asymptomatic

an immediate threat or may be predominantly fibrotic and calcific, in which event the danger is more remote. They may be stationary, retrogress-

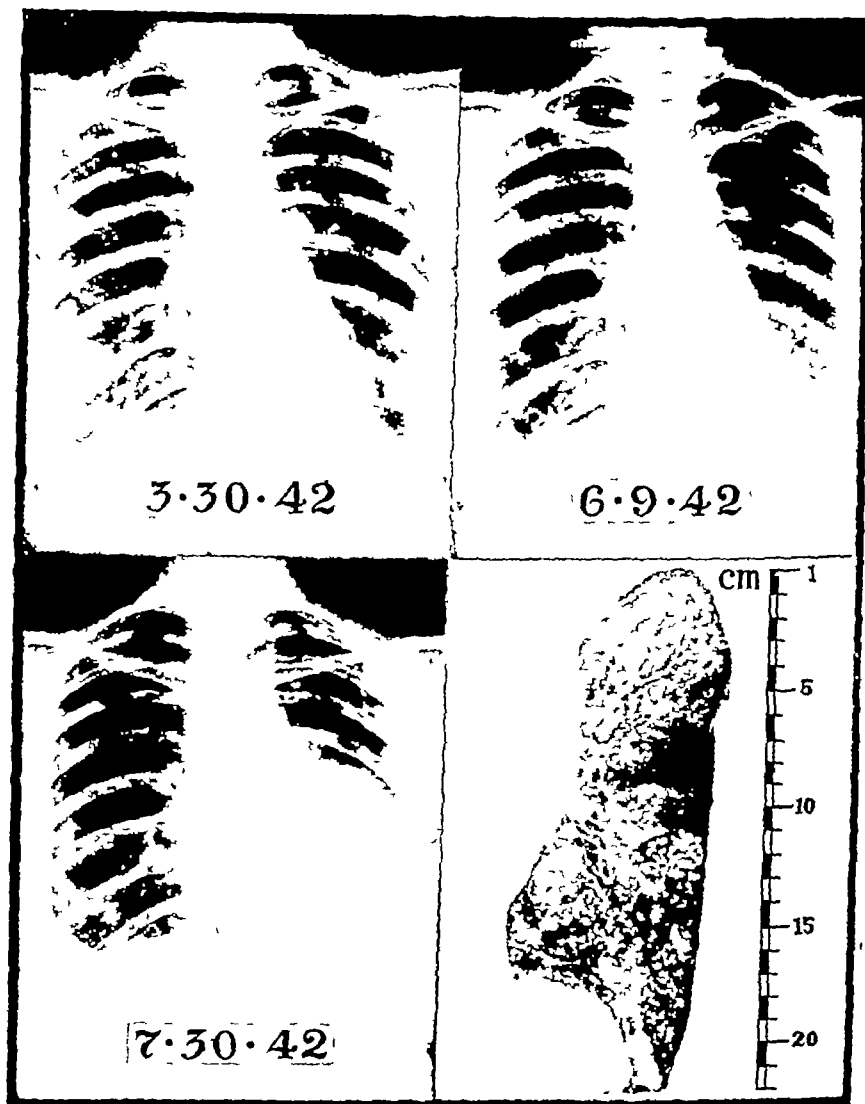


FIGURE 1 Case 2094

A 29-year-old, married woman, was first seen in March, 1942, complaining of fatigue, low-grade fever and wheezing in the left side of the chest of 3 months' duration. She had been treated for bronchitis with sulfadiazine. A roentgenogram of the chest taken at this time (upper left) revealed a small area of infiltration in the left 2nd interspace. A sputum examination was not performed, and the patient was advised to return in 3 months for another x-ray examination of the chest. A chest x-ray film taken June 9 (upper right) showed little, if any, significant changes, and the patient's symptoms and general condition had not changed since the time of her first examination three months earlier. In a film taken July 30 (lower left) just six weeks later, there was a mediastinal shift, and increased density at the left base was interpreted as atelectasis; the infiltration in the left upper lobe had also increased. The patient's symptoms had increased, and a bronchoscopy revealed a marked tuberculous ulcer stenosis of the left main bronchus, the sputum was positive. A left pneumonectomy was performed and the patient is living and well today, with a persistently negative sputum. In the surgical specimen (lower right) the entire left lower lobe was literally riddled with caseous nodules and numerous areas of caseation were also present in the upper lobe; there was no cavity. Comment: This case illustrates pulmonary tuberculosis masquerading as "asthmatic bronchitis." It also demonstrates rapid progression of disease within the space of a few weeks, which was the direct result of the bronchial lesion in this particular case. A sputum examination early in the course of the patient's illness would have established the diagnosis and would have brought her under proper treatment. This possibly might have averted the marked spread of the tuberculosis.

or produce extremely mild symptoms presents a serious and difficult problem. These lesions may form early exudative, caseous foci and thus carry

sive or progressive. The basic problem is that of proving the inactivity or activity of the demonstrated x-ray lesion. It becomes the duty of the

physician not only at once to guard patients with nocuous lesions against long periods of unnecessary therapy, but — what is more important — to protect those with active lesions by giving prompt and energetic treatment

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of early lesions are associated with no change in the leukocytic index and no elevation of the sedimentation rate, so that these laboratory tests are of value only when they show abnormality

### *Evaluation of the Roentgenogram*

It is evident that the clinical evaluation of the patient and the study of the sputum, leukocytic index and erythrocyte sedimentation rate establish the activity of the pulmonary lesion in some cases. An extremely important group remains in which

of the x-ray shadow strongly indicates the presence of activity. Most dense and homogeneous lesions with ill-defined, fuzzy edges are exudative. More frequently, the activity of the process is indicated by serial roentgenograms. Any change, whether it be progression or resolution, indicates an active lesion. It is essential to realize that such foci resolve to a point at which little or no change is discernible from month to month, and yet remain a constant threat because of residual foci of caseation. After the x-ray fails to reveal any change in the lesion it re-

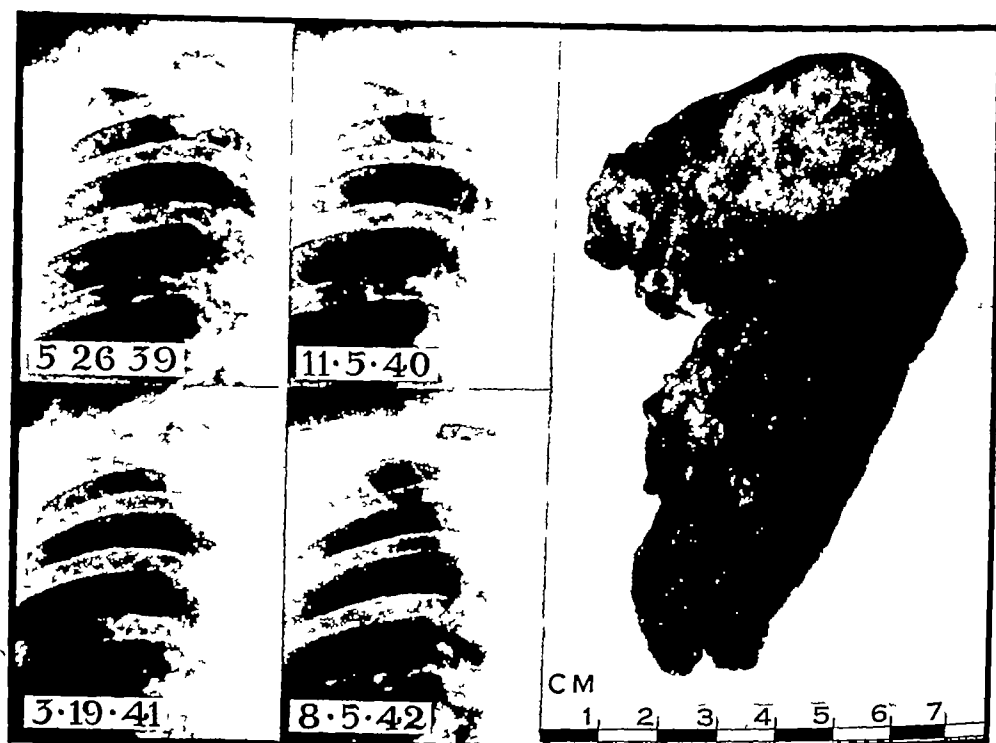


FIGURE 2 Case 2194

This 41-year-old single woman was first seen in October, 1942. A mass in the right upper lobe (upper left) had been discovered elsewhere in May, 1939 and had been followed by periodic chest x-ray films. The patient had always been asymptomatic. Repeated sputum examinations were negative, as was bronchoscopy. Bronchography revealed no distortion of the bronchi in the right upper lobe. The serial x-ray films (lower left) had shown a gradual increase in size of the mass, and an exploratory thoracotomy was advised. At operation on November 12, a large mass was found in the right upper lobe. No lymph nodes were palpable, but a few nodules were felt in the surrounding lung tissue. A diagnosis of tuberculoma was made, and a right upper lobectomy was performed. The patient had an uneventful postoperative course, and she is now asymptomatic, well and working. The surgical specimen (right) showed a large tuberculoma, and pathological examination revealed this mass to be incompletely encapsulated. Two areas of softening in the caseous mass were found, and numerous small tuberculous foci were seen in the surrounding parenchyma. The bronchial lymph nodes showed tuberculous involvement. Comment: This tumor in the right upper lobe was discovered by routine x-ray examination, but the diagnosis remained uncertain until proved at the time of exploratory thoracotomy.

the only significant evidence of trouble is the lesion demonstrated on the x-ray film. Once a single survey film has located an abnormal shadow, it is necessary to follow up this examination with a more comprehensive x-ray study. Fluoroscopy, stereoscopic exposures, spot films and oblique exposures often yield additional information. The precise location in respect to pulmonary segments should be determined, and the size and character of the abnormal shadow in all its dimensions should be known at the beginning. At times the character

quires months, and frequently years, for the processes of healing and fibrous encapsulation to become sufficiently firm to offer adequate protection against reactivation.

It cannot be too strongly emphasized that a minimal tuberculous lesion causing no symptoms, no abnormal physical findings and no alteration of the leukocytic index or erythrocyte sedimentation rate can be, and frequently is, an early focus of disease with serious potentialities and representing an immediate threat.

*treatment*

Needless to state any patient with a positive sputum or clinical evidence of activity requires immediate treatment. It is not the purpose of this discussion to consider in detail the various types of therapy; rather, because of the larger number of minimal lesions in the cases under discussion, it seems timely to restate the fundamental concepts of the treatment of the minimal and more particularly the early tuberculous lesion. The following concepts are not original but have been proved over and over again by many studies of the pathogenesis, pathology, resolution and clinical aspects of early tuberculous infiltrations.

The most opportune time to treat tuberculosis is during the phase of the early lesion when resolution and complete healing are more nearly possible and more easily accomplished than in any later phase of the disease process. The early infiltration tends to caseate and spread, and this is what happens in the majority of untreated cases. On the other hand, most cases treated by strict bed rest undergo resolution and healing.<sup>5</sup>

Progression of such an early minimal lesion may be extremely rapid, with moderately advanced or far-advanced disease resulting in as short a time as a few weeks.<sup>6</sup> The younger the patient, the greater is the possibility of rapid progression. Thus, any lesion in a teen-age person or a young adult should be considered active until proved otherwise by a long period of observation, during which frequent x-ray films should be taken at intervals not exceeding every two weeks. In any case, regardless of age, a policy of watching the lesion with the patient carrying on his normal activities is justifiable only when the lesion is fibrotic and inactive beyond any doubt. To wait for a minimal lesion to spread to prove its activity is to court disaster, for such a procedure not only lengthens and complicates the course of treatment but jeopardizes the patient's chances of recovery.

All patients with early tuberculous lesions should be treated promptly and energetically with strict bed rest, preferably in a sanatorium. The younger the patient, the more rigid and prolonged the treatment should be. The vast majority of early lesions resolve and heal with this treatment. If progression occurs, other measures, such as pneumothorax, may be indicated. It seems important to re-emphasize the need for x-ray films taken at intervals of one or two weeks during the first several months because such lesions may spread rapidly. Treatment should be continued for many months after all clinical, laboratory and x-ray evidence of activity have disappeared. This rule is based on the fact that the resolution and fibrous encapsulation of a tuberculous focus are slow processes and continue for at least a few years, during which time any factor that upsets the patient's general resistance is likely to cause an exacerbation.

In 1937, Amberson<sup>5</sup> reported his experiences with x-ray surveys and the treatment of pulmonary tuberculosis in student nurses at Bellevue Hospital, New York City, over a six-and-a-half year period. In this paper he told a story to which all physicians should listen attentively. They need look no further for the proper treatment of the early tuberculous lesion. Amberson states:

All tuberculosis appearing in student nurses has been discovered early, usually in the form of the early infiltration. Progression or relapse of the lesion in spite of rest treatment has occurred in less than 5 per cent of the cases. All who have completed treatment were able to work, and there have been no deaths from tuberculosis.

This study emphasizes the fundamentals of successful treatment of the early tuberculous focus — early discovery of the lesion and prompt, energetic and prolonged treatment, with bed rest and the judicious supplementary use of collapse measures.

## CARCINOMA OF THE LUNG

Carcinoma of the lung is a problem that should be of concern to every physician. Statistics show that it represents over 10 per cent of all cases of carcinomas coming to autopsy. In Koletsky's study<sup>7</sup> of 7685 autopsies, the lung was the second most frequent site of primary cancer, being exceeded only by the stomach. Jaffé<sup>8</sup> in a study of 6800 autopsies found it in the third place, with the stomach in the first place and the intestine in the second. All evidence points to an absolute as well as a relative increase in incidence. At least 15,000 people in the United States die each year from cancer of the lung.<sup>2</sup>

*Clinical Factors*

Carcinoma of the lung, like cancer elsewhere in the body, is a disease of later life, occurring most frequently in persons over forty years of age. It is, however, by no means rare in the fourth decade, and it is occasionally seen in younger patients. It is predominantly a disease of the male sex, being at least four times as frequent in men as in women.

Primary carcinoma of the lung is bronchiogenic in origin. Thus, the signs and symptoms are the results of three processes — local irritation and destructive processes in the bronchus itself, varying degrees of bronchial occlusion and secondary changes in the lung parenchyma. In the very early stages, when the degree of bronchial occlusion is small, the x-ray examination is likely to be negative, as is the physical examination. Although symptoms may be absent at such a time, experience has shown that they tend to occur quite early in the disease. Those oftenest seen at this stage are an irritative, nonproductive, persistent cough and hemoptysis, but localized wheezing is not infrequent. At times, a metastasis from a small tumor is the cause of the first symptoms noted. As the tumor enlarges and the degree of bronchial occlusion becomes greater, the x-ray and physical findings fre-

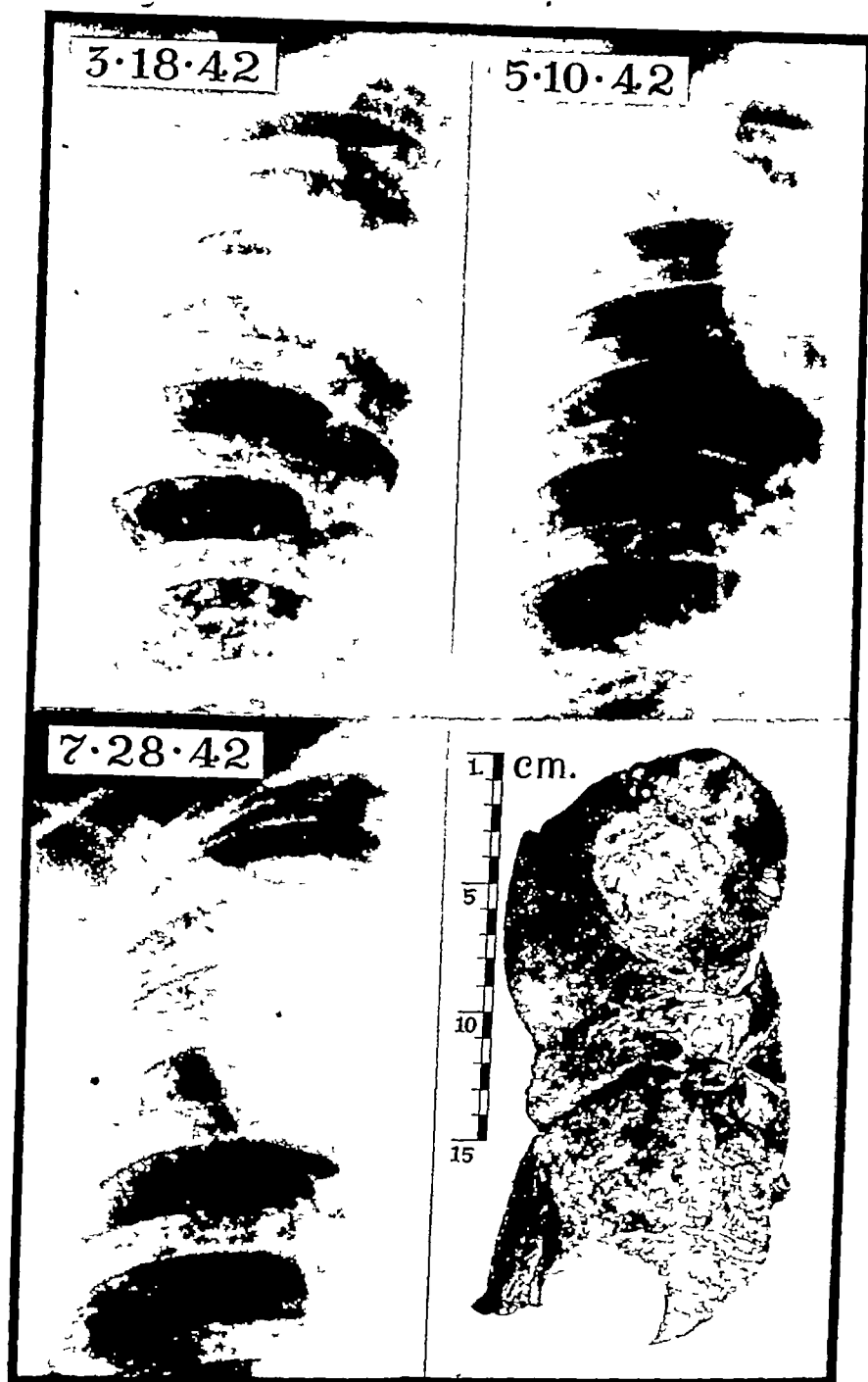


FIGURE 3 Case 2103

This 44-year-old man had complained of slight cough for several years, which was attributed to excessive smoking. In March, 1942, the sputum became blood-streaked. On the basis of the roentgenogram taken on March 18 (upper left), a diagnosis of pulmonary tuberculosis was made in spite of a persistently negative sputum. A roentgenogram taken two months later (upper right) showed progression of disease. The sputum was still negative, but the patient was still being treated for pulmonary tuberculosis. On the basis of a roentgenogram taken on July 28 (lower left), four months after the initial roentgenogram, a diagnosis of tumor was made, and the following month the patient was referred for surgical treatment. Bronchoscopy was negative. Exploratory thoracotomy revealed a large tumor in the right upper lobe, with metastases to the bronchial lymph nodes. No mediastinal nodes were palpable. A palliative right pneumonectomy was performed. The patient made an uneventful recovery and remained well until December, when he developed evidences of metastatic disease, with death in February, 1943. The surgical specimen (lower right) was a Grade III epidermoid tumor, with metastasis to the bronchial lymph node. At the time of autopsy, metastases were found in the spleen, the left adrenal gland and the peritracheal and supraclavicular lymph nodes. Comment: This case demonstrates bronchiogenic carcinoma was quering as pulmonary tuberculosis in its early stages. The persistently negative sputum, with a changing x-ray lesion, should have aroused suspicion and indicated further diagnostic procedures. An exploratory thoracotomy at the time of the first roentgenogram would have settled the diagnosis, and pneumonectomy would have offered a better chance of cure. Attention is called to the fact that bronchoscopy was negative even at the time of operation, when metastases had already occurred. This emphasizes the limitations of bronchoscopy in the early diagnosis of bronchiogenic carcinoma and the necessity for exploratory thoracotomy.

uently indicate an obstructive emphysema of lobular, lobar or multilobar extent. More complete bronchial occlusion leads to atelectasis of similar segments of the lung. If this persists superimposed infection of the involved parenchyma is the rule.

The x-ray manifestations depend on four factors — the type and location of the tumor, the degree of bronchial occlusion, whether infection of the parenchyma has occurred and whether mediastinal or chest wall extension has taken place. In the early stages, the most frequent x-ray findings are obstructive emphysema or atelectasis of lobular, lobar or multilobar extent. Less often, the tumor itself is seen — notably when it has originated in the periphery of the bronchial tree. Evidence of infection may be superimposed early. Extension to the mediastinum and chest wall, although certainly not a part of the early pathologic life of the tumor, sometimes occurs early in the clinical course.

From this incomplete consideration of bronchiogenic tumors, it can be seen that most of the symptoms usually listed as those produced by carcinoma of the lung, such as pain, excessive sputum, weight loss and cachexia, are as a rule not a part of the early picture. They are the result of extension of the tumor, secondary changes of lung parenchyma and the systemic reaction to both these processes. More frequently, the x-ray film shows definite changes, yet the symptoms are so mild as to cause little suspicion of such a serious underlying lesion. The latter type of case is the one oftenest seen in the early stages in survey work and clinical practice, and is the one on which we wish to focus attention. Most patients are men past middle age with a demonstrated x-ray lesion, accompanied by no symptoms or by mild ones. In many cases the only symptom is a mild cough, which is attributed to cigarette smoking. The clinical picture may mimic that of any of the ordinary diseases of the lungs. The x-ray manifestations may be indistinguishable from those of tuberculosis, bronchiectasis, unresolved pneumonia or suppurative disease. Such patients present a serious problem and one that demands immediate solution. If the lesion is caused by carcinoma, speed in diagnosis and surgical extirpation offer the only chance for cure. In no other disease process is time so dangerous an enemy. Early diagnosis and radical treatment in the early stage frequently lead to successful therapy. Without exception a policy of watchful waiting leads to ultimate death.

Thus, any patient, especially one past middle age, with persistent pulmonary symptoms or an unexplained x-ray lesion\* should be immediately subjected to a series of diagnostic tests to prove or disprove the existence of cancer. Whenever

possible, tissue should be secured for pathological study, since this is the only sure way to establish the diagnosis.

### Diagnostic Procedures

*Search for peripheral metastasis.* Careful examination of the cervical lymph nodes and the skin for evidence of metastasis should be made, and suspicious nodes or skin nodules should be removed for pathological study. If the biopsy is positive the diagnosis is proved and further studies are unnecessary. If there is no evidence of peripheral metastases, bronchoscopy should be the next procedure.

*Bronchoscopy.* Now that a greater number of cases of early bronchiogenic cancer are being discovered by chest roentgenograms, a revision of the present concept of the value of bronchoscopy as a diagnostic procedure is in order. The medical literature abounds with statistics indicating that 70 to 75 per cent of all bronchiogenic carcinomas originate in the major bronchi and are thus visible through the bronchoscope and accessible for biopsy.

These statistics are misleading in that they apply to all types of tumor without regard to time relations. They are false when applied to early carcinoma of the bronchus. As Gebauer<sup>9</sup> has shown, bronchoscopy if performed early yields negative results in 40 per cent of the cases because the site of origin is beyond bronchoscopic view. In addition to the time relation, the percentage of positive biopsies varies with the type of tumor. For instance, Gebauer demonstrated that 49 per cent of squamous-cell carcinomas originate in the upper lobes or small branch bronchi and that they are not likely to be accessible for biopsy until rather late in the disease. When one considers that epidermoid carcinoma is not only the most frequent but the most curable of all types of lung cancer, the significance of this finding can be realized.

Thus, the actual value of bronchoscopy in the early diagnosis of carcinoma of the lung can be stated in simple terms as follows. It still is the most valuable diagnostic procedure for securing tissue for biopsy. It is, however, an unreliable guide when the results are negative, since it does not in any way exclude the presence of a tumor immediately beyond the vision of the bronchoscopist. A negative bronchoscopy in a patient suspected of having pulmonary cancer thus means only that further diagnostic procedures are indicated. It cannot be emphasized too strongly, since it is a fact not generally recognized, that in the diagnosis of early cancer bronchoscopy is about 50 per cent inefficient.

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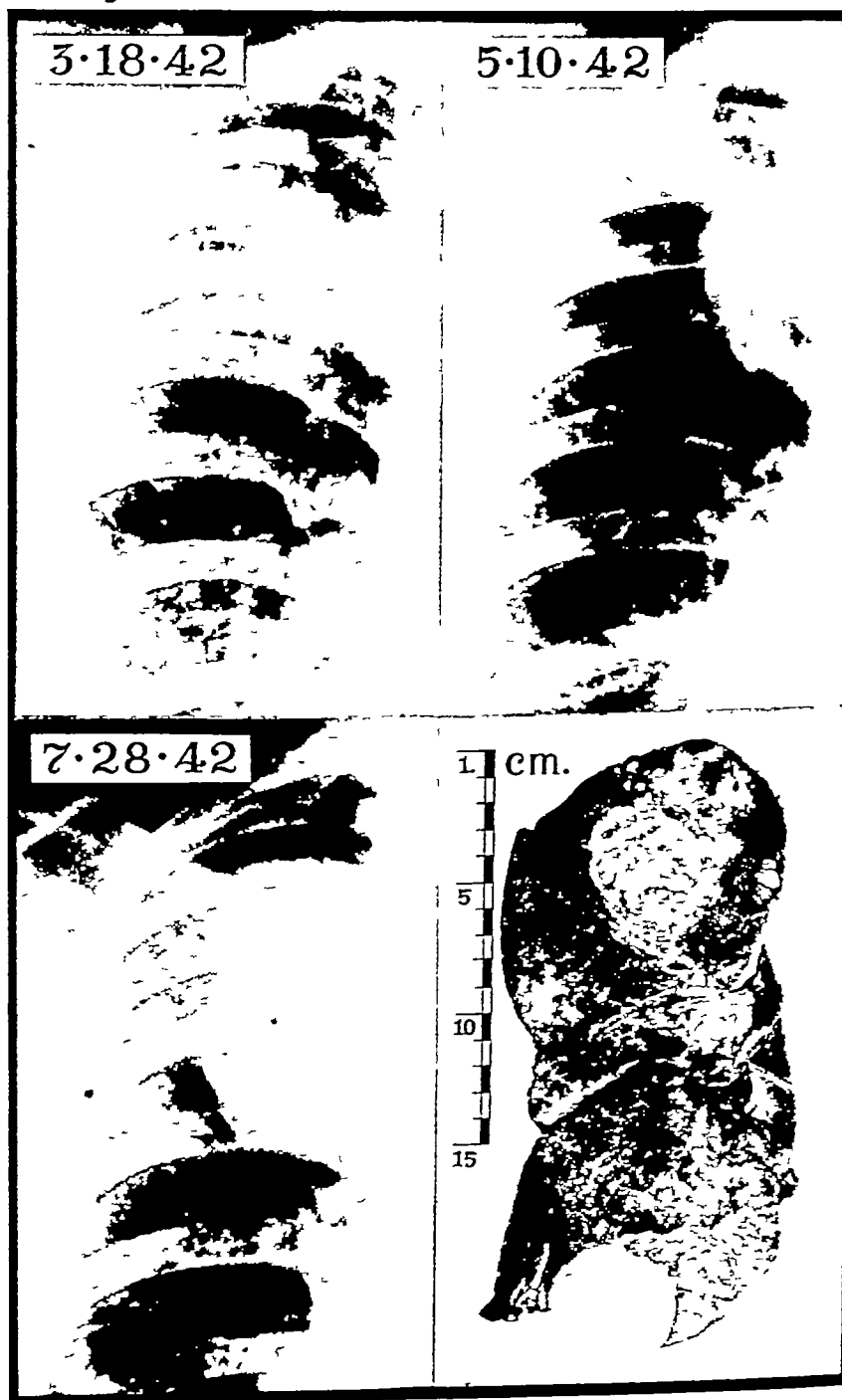


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bronchoscopy is needed to obtain a biopsy specimen. Study of sputum for malignant tissue. In the experience of most workers, and especially those in



FIGURE 4 Case 1268

This 55-year-old man was first seen on November 24, 1940, at which time he had been under treatment for pulmonary tuberculosis for six months. His history revealed that six months previously he had had a "pneumonia" followed by a chronic cough and expectoration. In spite of a persistently negative sputum, a diagnosis of pulmonary tuberculosis was made, and the patient sent to a sanatorium, where he remained under treatment for six months. While there, his sputum was also negative on all tests. When first seen in November, his weight had dropped from 115 to 95 pounds. He complained of cough, expectoration of blood-streaked sputum, night sweats, and a dull pain in the right shoulder. Bronchoscopy revealed a mass protruding from the orifice of the right upper lobe, but biopsy of this revealed only necrotic tissue. Exploratory thoracotomy was performed. A large tumor was found in the right upper lobe. One mediastinal lymph node was enlarged, and frozen section of this revealed epidermoid carcinoma. A palliative pneumonectomy was performed. The patient did well for a few months and then rapidly became worse, dying in November, 1941. The roentgenogram taken just before operation (upper) suggests pulmonary tuberculosis, there being no indication of the large tumor mass found in the surgical specimen (lower). Comment: The chest roentgenogram in this case suggested pulmonary tuberculosis. The clinical course and the persistently negative sputum, however, should have indicated bronchoscopy and exploratory thoracotomy six months before the patient was referred for these procedures. It is possible that a curative type of pulmonary resection might have been performed at that time.

believe that bronchography should never be performed unless the results of bronchoscopy are negative because even if it demonstrates the tumor,

the average laboratory, the demonstration of cancerous tissue in the sputum has proved to be extremely disappointing. It is not recommended

a routine diagnostic procedure in cases suspected being cancer. If it is used, it is of significance only when positive.

**Aspiration biopsy.** Aspiration biopsy is not without danger and should be used only in cases that are obviously inoperable, especially when the tumor is located peripherally. In cases considered operable, it seems to be unnecessary. A positive aspiration biopsy calls for surgical exploration to determine resectability. A negative one does not

diseuse for exploratory thoracotomy. For many years abdominal exploration has been an accepted procedure in establishing the diagnosis of unexplained tumor masses and lesions in the abdominal cavity. It is essential that physicians develop a similar attitude toward exploratory thoracotomy, if it is ever to be possible to treat a large proportion of cases of pulmonary cancer in the early stages. The value of this procedure can be gleaned from the fact that in 24 per cent of 153 cases reported

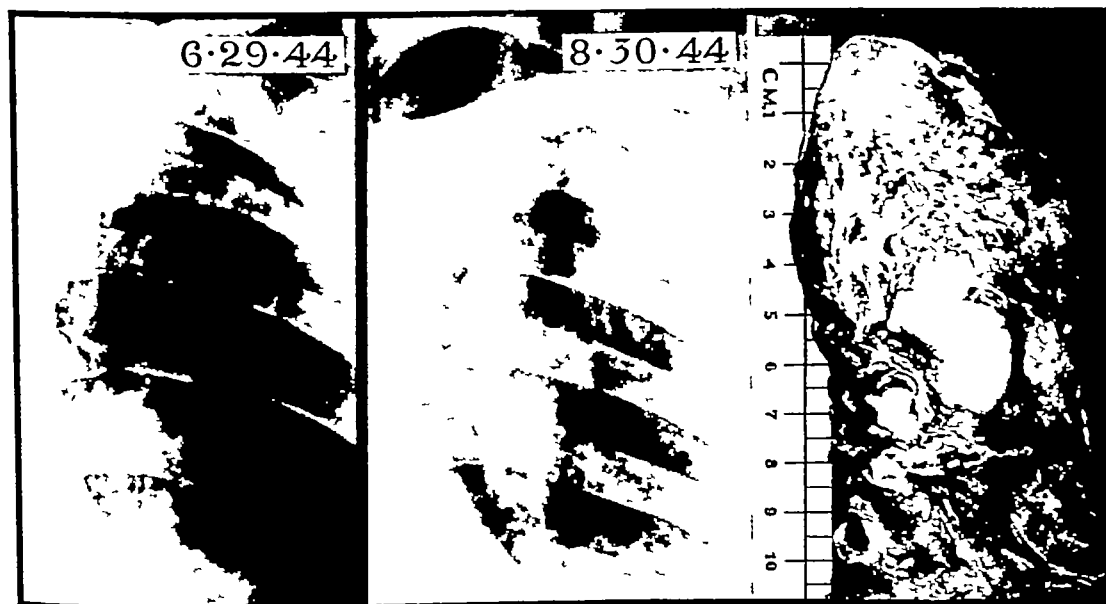


FIGURE 5 Case 3085

This 52-year-old man was first seen on June 17, 1944, at which time he complained of a slight cough and expectoration, afternoon fever and an intermittent dull pain just below the angle of the left scapula. A chest roentgenogram (upper) revealed an area of increased density at the left hilum and an infiltration in the left upper lobe. Bronchoscopy was negative. Bronchiogenic carcinoma was suspected and exploratory thoracotomy was about to be advised when the laboratory reported finding acid-fast bacilli in the sputum. The sputum was then cultured and a guinea pig inoculated. These proved to be negative. A chest roentgenogram taken just before operation (middle) showed slight clearing of the infiltration in the left upper lobe. Exploratory thoracotomy was performed on September 1 and a tumor was found in the left upper lobe near the hilum. There were also considerable induration and suppuration of the lung tissue peripheral to the tumor. The surgical specimen (right) showed a large tumor (carcinoma, unclassified) near the hilum as well as metastases to a bronchial lymph node. There was involvement of the parenchyma by infection distal to the tumor. Comment: This case illustrates several interesting points. First the symptoms were extremely mild. Second, the finding of acid-fast bacilli delayed exploratory thoracotomy and if the laboratory report had been relied on the patient might have been subjected to treatment for pulmonary tuberculosis. Third, the chest roentgenogram gave little evidence of the presence of the tumor itself, in spite of its size. In this respect it resembles Case 1268. The findings in these two cases emphasize the limitations of a routine posteroanterior roentgenogram. Stereoscopic, lateral and even oblique views should supplement the posteroanterior film in all cases with pulmonary disease. Finally, exploratory thoracotomy was the only diagnostic procedure that could possibly have established the diagnosis.

rule out tumor, and therefore surgical exploration must be done to settle both the diagnosis and the question of operability.

**Exploratory thoracotomy.** Exploratory thoracotomy in suspected cases of tumor is a procedure that is used too little and too late. With the present-day status of thoracic surgery, this operation is on a par with abdominal exploration regarding safety and accuracy. In spite of this, there is still a great deal of hesitancy on the part of the average physician to refer a patient with unexplained pulmonary

by Overholt<sup>10</sup> in 1942, the diagnosis was established and treatment was carried out on the basis of a biopsy specimen secured at exploratory thoracotomy. The sooner the pathologic process is discovered, the more valuable as a diagnostic procedure exploratory thoracotomy becomes. We believe that it should be carried out immediately to establish the diagnosis in all patients suspected of having pulmonary cancer, even though the bronchoscopy is negative, except of course, for those with proved metastasis. This concept is based on three es-



sential facts First, it is a safe procedure. Second, it is an efficient procedure and establishes the diagnosis in the vast majority of cases when cancer exists Lastly, the diagnosis can be established at the operating table by frozen section, the operability determined, and the indicated operation carried out immediately

### MEDIASTINAL TUMORS

The problem of mediastinal tumors is one of increasing importance, for mass surveys show that

The mediastinum is the site of many different types of primary tumor, because of the varied type of tissue present and the complexity of embryologic development of the contained organs From a pathological standpoint, mediastinal tumors present an extremely complex problem The clinical approach and treatment are, however, fairly well standardized

The problem with which we are now concerned is that of a patient whose mediastinal tumor has been discovered on the roentgenogram The

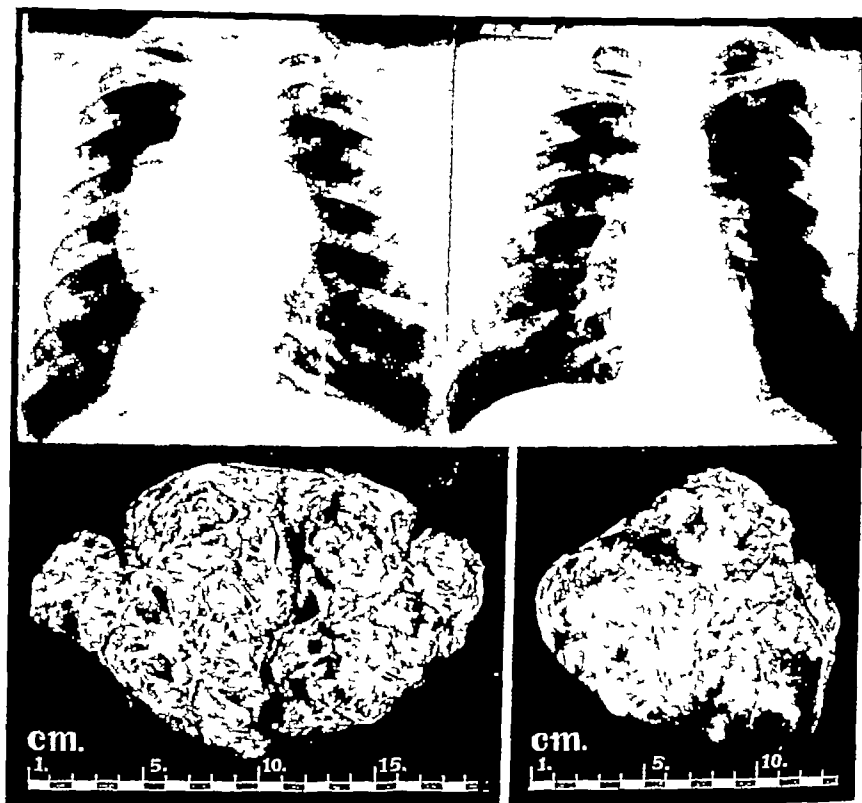


FIGURE 6 Case 2704

This 20-year-old man received a medical discharge from the Marine Corps because of a mediastinal tumor that had been discovered in routine x-ray examination He was in excellent health and entirely free of symptoms The preoperative roentgenogram (upper left) showed a large mediastinal tumor protruding to the right and left of the mediastinum Lateral views had shown that the tumor was in the anterior mediastinum A preoperative diagnosis of a teratoma was made The tumor was removed on December 9, 1943, the patient made an uneventful recovery and has remained well A chest roentgenogram taken ten months following operation (upper right) was essentially normal Examination of the surgical specimen (lower) proved the tumor to be an adenocystoma of respiratory epithelium Comment This case illustrates the size to which a mediastinal tumor can grow and cause absolutely no symptoms

they are much more frequent than has been suspected from previous clinical and autopsy data The incidence of mediastinal masses in a recent survey conducted by the United States Public Health Service<sup>11</sup> was 0.012 per cent Bloch and Tucker,<sup>12</sup> using routine fluoroscopic examination for all patients admitted to the University of Chicago clinics, found an incidence of mediastinal and diaphragmatic lesions of 0.57 per cent When the large number involved in such surveys is considered, the magnitude of the problem becomes evident

vast majority of those discovered in surveys cause either no symptoms or those so mild that they occasion little concern to the patient The physician must answer two questions what the nature of the mediastinal mass is, and how it is to be treated

Localization is of the utmost importance in determining the type of tumor The most frequent tumors of the posterior mediastinum are those arising from the sympathetic ganglions — ganglioneuromas — or the spinal nerves — neurofibromas The tumors oftenest found in the anterior medi-

stinum are dermoid cysts, teratomas and malignant lymphomas, such as lymphosarcoma, Hodgkin's disease and leukemic lymphoma. It is therefore important to determine, if possible, whether the tumor is benign or malignant. The x-ray appearance helps to determine this. Benign tumors grow slowly and are usually oval or circular, quite dense, and sharply delimited laterally from the lung. Malignant tumors grow rapidly and are not so likely to be so smooth and discrete, but rather tend to be lobulated and less sharply defined from the

### Treatment

Statistics and experience show that the vast majority of benign mediastinal tumors eventually cause death because of malignant degeneration, infection or mechanical pressure on vital structures in the mediastinum. It is generally agreed that surgical extirpation is the proper treatment. Successful removal is the rule. The mortality is extremely low, especially if the operation is performed when the tumor is small and before any secondary changes have occurred.



FIGURE 7 Case 3301

This 34-year-old married woman applied in October, 1942, for a position in a hospital where a pre-employment physical examination, including an x-ray film of the chest, is routinely required. The survey film (right) showed an area of increased density at the right base. Bronchoscopy was immediately performed, and an early primary adenocarcinoma of the right main-stem bronchus was found. Before the end of the same month that the survey film was taken, the chest was explored and an operable lesion was found. The surgical specimen (left) showed adenocarcinoma of right lower lobe bronchus, with indurative pneumonia distal to the occlusion. The lymph nodes were negative. Convalescence was satisfactory, and the patient has remained free of symptoms. Comment: This patient will probably be cured of a cancer for two reasons — first, because of the policy of one institution to require pre-employment chest x-ray films and, second, because of prompt investigation and treatment. If she had waited for symptoms to appear it might have been too late. If an explanation for the abnormal survey film had not been sought immediately, it might have been too late. Fortunately for this patient the disease was apprehended when it was silent yet early, the potential danger of the lesion being fully appreciated.

pulmonary tissue. Cervical or axillary nodes are frequently associated with malignant lymphomas, and biopsy may prove the diagnosis. In case of doubt, a therapeutic test dose of x-ray helps to prove the nature of the tumor. Malignant lymphomas respond rapidly to x-ray therapy, whereas benign tumors are unaffected by it. In dermoids and teratomas, heavy-exposure roentgenograms with the Potter-Bucky diaphragm may reveal teeth or bone in the tumor. Fluoroscopy and roentgen-lymngraphy assist in ruling out aneurysm

With these facts in mind, the treatment of mediastinal tumors can be expressed simply as follows. Surgical extirpation is indicated in benign tumors. An exception to this rule is a benign tumor in an elderly patient that is causing no symptoms. We advise frequent x-ray examination in such cases. So long as the tumor remains unchanged, no therapy is offered, but if it increases in size or causes symptoms, surgical removal is advised. In anterior mediastinal tumors, when there is doubt concerning the nature of the tumor, a therapeutic test dose

of x-ray is advised. If a response is noted, the tumor is considered to be a malignant lymphoma and x-ray therapy is continued. If the tumor fails to respond within four to six weeks, surgical exploration is advised. It is then important to proceed with excision without delay to avoid technical difficulties resulting from the effects of x-ray on local tissue.

### SUMMARY AND CONCLUSIONS

Thousands of intrathoracic lesions are being discovered in mass x-ray surveys of the population. These patients are being referred to physicians in rapidly increasing numbers for evaluation and treatment.

Many lesions are in the early stage, when symptoms are either absent or so mild that the life-threatening lesion is unsuspected by both the patient and his physician. The immediate identification of the lesion and the institution of proper treatment during this stage offer the patient his best chance to get well. Delay may either rob him of an opportunity to have curative treatment or introduce factors that prolong or complicate such treatment. A significant proportion of all lesions discovered in survey work carry a definite threat to the patient's health and life.

A policy of watchful waiting until symptoms or extension forces the issue will not raise the percentage of salvages in either tuberculosis or cancer of the lung. The full value of survey work will not

be realized unless a proper disposition of all uncovered lesions is made.

The medical profession is faced not only with the obligation but also with the privilege of evaluating chest disease in advance of the time when most patients ask for help — after progressive disease has caused symptoms. The potentialities of this type of preventive medicine are great. The profession has within its grasp the power to overcome the plague of tuberculosis and to tear the label of certain death from cancer of the lung.

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# HOMOLOGOUS SERUM JAUNDICE FOLLOWING THE ADMINISTRATION OF COMMERCIAL POOLED PLASMA\*

## A Report of Eight Cases including One Fatality

CHARLES M. GROSSMAN, M.D.,† AND ERNEST W. SAWARD, M.D.‡

VANCOUVER, WASHINGTON

ALTHOUGH the occurrence of homologous serum jaundice has been repeatedly reported since 1937<sup>1-14</sup> the interest in this condition became widespread following its high incidence in American troops vaccinated against yellow fever in 1942.<sup>15</sup> The reports of Beeson<sup>16</sup> and others<sup>17, 18</sup> gave evidence of the occurrence of the disease following transfusion with whole blood or plasma. A recent report by Rappaport<sup>19</sup> indicates that this sequela may not be infrequent in the armed forces. At present there are few reports of hepatitis in civilian hospitals following the administration of whole blood or plasma, although one might expect its occurrence to be frequent in view of the large amounts of plasma available for civilian distribution. In no reports have we seen any autopsy data although such information in cases of hepatitis due to homologous serum used with immunizing agents has been recorded.<sup>14, 20</sup> The present report has been made to add to these data.

The discharge diagnoses of infectious hepatitis and catarrhal jaundice listed in the Northern Permanente Foundation Hospital files for September, 1943, to September, 1945, were reviewed with the object of separating all cases of homologous serum jaundice. Eight such cases appeared to satisfy the diagnostic criteria. One of these terminated fatally, and the autopsy findings are available for review.

It is recognized that any or all of these cases may represent a spontaneously occurring attack of infectious hepatitis. This criticism is, however, true of the other cases reported in the literature since there are no specific diagnostic criteria distinguishing these two conditions at the time when the hepatitis is present, the clinical and laboratory findings being identical. The etiologic agents of the conditions have many capabilities in common, such as those of passing through bacterial filters, of surviving temperatures as high as 56°C for a similar length of time and of being transmitted to new human hosts. Neither agent has successfully induced the disease in experimental animals, and the only known difference between them seems to be that relating to the incubation period. In homologous serum jaundice this is approximately fifty days to four months, whereas in infectious hepatitis

it is usually less than fifty days. Another possible difference is that of ease of transmission, since the former is apparently more difficult to transmit by the oral and nasopharyngeal routes than the latter.<sup>21-24</sup>

## CASE REPORTS

**CASE 1** E. P., a 31-year-old state highway patrolman, was admitted to the Orthopedic Service on March 14, 1945, and was operated on the same day for a simple fracture of the femur with a Roger-Anderson pin fixation. He was given 250 cc of plasma on the day of operation. On May 26, after running an irregular low-grade fever for 12 days, he developed generalized aching pains, anorexia, nausea and vomiting. Jaundice was noted clinically for the first time on May 30, at which time the icteric index was 55. It rose to 70 on June 4 and fell to 14 on June 21. By June 16, the patient was asymptomatic except for the fracture.

**CASE 2** A. S., a 62-year-old engineer, was admitted to the Orthopedic Service on October 19, 1943, for a compound fracture of the tibia. He was operated on with the Roger-Anderson pin technique, and on the same day was given 250 cc of plasma. He was discharged on November 6, but he was readmitted on January 22, 1944, with a history of epigastric distress, nausea and vomiting of 2 days' duration. The urine was dark and the stool was clay-colored. A tender liver edge was palpated on examination. The patient was obviously icteric, the index being 74. He was discharged asymptomatic on February 4, the icteric index having fallen to 41.

**CASE 3** C. H., a 39-year-old rigger, was admitted to the Orthopedic Service on September 3, 1944, for a compound fracture of the left tibia and fibula. This was reduced by operation with the Roger-Anderson pin technique. On the day of admission he was given 250 cc of plasma. Manipulation of the fracture was done on September 25 and October 18. On October 20, anorexia developed. There was a brief episode of diarrhea at that time. On October 31, the icteric index was 26. By November 20, the icteric index was 84, but the patient was asymptomatic. By November 30, it had dropped to 25. There were no further symptoms.

**CASE 4** M. N., a 27-year-old woman, a hospital employee, was admitted to the Gynecological Service on June 29, 1944, for perineal repair and a vaginal hysterectomy, at which time 250 cc of plasma was given. Recovery was uneventful. On October 13, the patient was admitted to the Medical Service because of jaundice. She gave a history of epigastric distress and abdominal discomfort since October 1, dark urine, first noted on October 3, and clay-colored stools on October 13. The icteric index on October 14 was 66. The patient improved on symptomatic therapy and was discharged on October 27. On November 10, the icteric index was still 18.

**CASE 5** M. W., a 23-year-old woman, a painter's helper, was admitted to the Medical Service on June 4, 1944, in diabetic coma. As part of her therapy she received 250 cc of plasma. Recovery was uneventful and she was discharged but was readmitted on September 4 complaining of abdominal pain, diarrhea of 3 days' duration and nausea and vomiting for 1 day. She was obviously jaundiced, the icteric index being 50. She improved rapidly on symptomatic therapy. On September 18, the icteric index was 18.

\*From the Medical Service of the Northern Permanente Foundation Hospital.

†Chief Medical Service, Southern Permanente Hospital, Fontana, California.

‡Chief Medical Service, Northern Permanente Foundation Hospital, Vancouver, Washington.

**CASE 6 A B**, a 39-year-old woman, a sheet metal worker, was admitted to the Medical Service on February 1, 1945, with lobar pneumonia and shock, for which she was given 250 cc of plasma. She was discharged asymptomatic on February 7, but was readmitted on March 26 complaining of nausea and anorexia of 1 week's duration. On March 26, the icteric index was 48, the stools were clay-colored, and there was some bile in the urine. On April 11, the icteric index rose to 110. By April 16, it was 28. The patient was asymptomatic at that time and was discharged.

**CASE 7 T D**, a 50-year-old shipwright, was admitted to the Medical Service on October 11, 1944, for pneumonia due to a Type 2 pneumococcus, with subsequent effusion. He had a history of duodenal ulcer. On October 11, he was given 250 cc of plasma. On October 27, he was discharged asymptomatic. On February 22, he was readmitted because of gastrointestinal symptoms, which were attributed to the duodenal ulcer, and a subtotal gastrectomy was contemplated. On March 5, however, the icteric index was 35. The jaundice increased, and since the question of obstruction of the common duct was raised, exploration was performed on March 12. At operation the liver was slightly enlarged, pale and brown, without evidence of a metastatic lesion. The stomach was normal except for a small, firm mass with some scarring on the anterior surface of the pylorus. The head of the pancreas was indurated, and there was considerable edema of the surrounding tissues. The gall bladder appeared slightly edematous. The common duct and cystic duct were normal. At the time of operation the surgeon was unable to explain the symptomatology, and in view of the jaundice a subtotal resection was not done. The icteric index rose to 90 on March 14 and then gradually subsided. Following the operation, the gastrointestinal symptoms subsided, and the patient was discharged improved.

**CASE 8 I M**, a 55-year-old sheet metal worker, was admitted to the Medical Service on March 13, 1945, for pneumonia of the right lower lobe due to Type 1 pneumococcus. He was given 250 cc of plasma, in addition to the usual chemotherapeutic and supportive measures. After a rather stormy course, he improved considerably and was well on discharge on April 8. He was readmitted on May 5 with acute tonsillitis and evidence of a recurrence of the lobar pneumonia, and was treated for 5 days, with a prompt response to penicillin therapy. He was again readmitted on June 5, 1945. At that time he stated that he had had a shaking chill, muscular pain, weakness and a nonproductive cough of 2 days' duration. The temperature was 103°F. Physical examination was essentially negative. The white-cell count was 4300, with 62 per cent neutrophils. The urine was normal except for a slight trace of albumin. On June 8, jaundice was first noted clinically. The icteric index was 70 on June 9 and rose to 90 on June 11. The prothrombin time on June 11 was 6 minutes (control, 30 seconds). The patient became irrational on June 10, and then comatose. He went progressively downhill and expired on June 12 in spite of supportive therapy.

**Autopsy.** The organs were deeply jaundiced, and numerous subpleural and subepicardial petechial hemorrhages were found. The liver was of normal shape but was somewhat decreased in size, measuring 20 by 20 by 5 cm. Its surface was smooth and dark in color. It was pliable and flaccid, but cut with increased resistance. On the cut surface was seen a distinct pattern of dark-red dots and small lines on a greenish-ochre background. Several large, edematous periportal nodes were found. The spleen measured 14 by 9 by 4 cm. The capsule was tense and pale gray. On the cut surface the splenic parenchyma appeared deep red and congested and was firm, and the trabecular pattern was prominent. Malpighian corpuscles were not seen. The gall bladder was normal and contained some dark-green bile. Its ducts were patent.

Microscopically, sections of the liver showed the capsule to be intact. In large areas no liver cells were found. Those that remained were either in the periportal areas or at the periphery of the liver lobules. In place of the liver cells only the somewhat dilated capillaries remained. Numerous large, pigment-laden macrophages were scattered throughout the liver, and there was infiltration with lymphocytes and plasma cells and occasional polymorphonuclear leukocytes throughout the sections. The periportal areas contained dense accumulations of lymphocytes. Several sublobular veins were found that exhibited marked phlebitis. Their walls were in-

filtrated with inflammatory cells, which pushed the endothelium into the vessel lumen, and small areas of necrosis were seen. The bile ducts in the periportal spaces were of normal appearance and showed no attempt at regeneration. The liver cells, when preserved, were finely vacuolated and were undergoing necrosis. Very rarely, large liver cells or those containing two nuclei were found. Sections of the spleen showed distinct malpighian corpuscles. The pulp was deeply hyperemic. Sections of the lymph nodes revealed that all sinusoids were markedly dilated and contained large amounts of lymphocytes, plasma cells and polymorphonuclear leukocytes. The reticulum cells were somewhat increased.

The final anatomical diagnoses were acute necrosis of the liver and congestion of the spleen.

All these patients had negative histories with regard to drug or alcohol ingestion and exposure to toxic substances. X-ray examination of the abdomen was negative in every case. No patient had evidences of anemia.

## DISCUSSION

It will be observed that these patients had incubation periods ranging from fifty-four to one hundred and thirty-nine days, which conforms with the incubation period of the experimentally induced disease. It should be noted that the patients in Cases 1 and 3 were in the hospital throughout the time between the administration of plasma and the development of hepatitis.

In no case was there known occurrence of hepatitis in any of the members of the patient's family, nor was there any known contact incidence in the hospital. Among the 77 cases of infectious hepatitis studied at this hospital in the same two-year period, 13 (17 per cent) members of the patient's family had or subsequently developed jaundice.

None of the patients were seriously ill except the one in Case 8. The autopsy findings in this case differed in no way from those in cases ending in death following hepatitis due to the administration of yellow-fever vaccine,<sup>14 20</sup> nor are the findings different from those in deaths from infectious hepatitis.<sup>28</sup> In the absence of a biopsy, the operative report in Case 7 supplied no significant information, although the findings are not without interest.

During the two-year period during which these cases were observed, five hundred and one transfusions of commercial pooled plasma were administered. The plasma was purchased from a commercial manufacturer with nationwide distribution facilities, who states that each pool consists of at least fifty samples. The occurrence of 8 cases gives an incidence of 2 per cent, but this represents a minimal rather than a true incidence, since many patients received more than one transfusion and since patients who developed hepatitis were treated as outpatients or by physicians elsewhere did not come to our attention. Furthermore, patients who did not develop clinical jaundice but nevertheless had the clinical features of acute hepatitis, such as nausea, vomiting, anorexia and malaise, were not included. For example, we observed one patient with these symptoms and an icteric index of 15

ninety days after a transfusion of whole blood whose case suggests this possibility. Rappaport<sup>19</sup> has included 2 such cases in his report.

The true incidence of this condition is not known at the present time. Reports in the literature vary from as many as 26 of 47 cases receiving pooled serum in one instance<sup>13</sup> to ten thousand transfusions of pooled plasma without any recorded evidence of homologous serum jaundice,<sup>26</sup> although in the latter report the authors state that their method may not have supplied complete data. The reasons for this discrepancy are manifold. Since there is a relatively high incidence of infectious hepatitis at the present time, it is only natural to attribute any example of this clinical picture to spontaneously occurring agents. The long incubation period of homologous serum jaundice separates the disease from the etiologic event by such a long period that causal relation may be overlooked. Finally, many physicians may not be alert to this possibility because of the absence of information about this condition in the literature until the last few years.

The incidence of this disease is undoubtedly becoming greater because of the increased use of commercially pooled plasma in cases in which transfusion of whole blood from a single donor was formerly used. Our experience has confirmed this since nearly one thousand whole-blood transfusions were given at this hospital in the same two-year period with no case of manifest jaundice. The chance of the etiologic agent's being given in any blood plasma therapy is many times increased as pools of fifty or more donors are mixed. The amount of icterogenic plasma necessary to contaminate a pool is minimal, since the disease can be transmitted by as little as 0.1 cc.<sup>13, 21, 22</sup>

In view of the disability<sup>27</sup> and the chance of fatality in homologous serum jaundice, the use of pooled plasma is not without danger. The fact that the icterogenic agent is not destroyed by drying and prolonged storage<sup>23</sup> makes the tracing of the icterogenic sample difficult. Since it has been reported that the agent is destroyed by ultraviolet radiation,<sup>21</sup> perhaps the hazard from the use of pooled plasma could be obviated by such a method.

#### SUMMARY

Eight cases of hepatitis with jaundice following the use of commercial pooled plasma are presented, 1 of these being a fatal case, with autopsy data available.

The factors relating to the apparent incidence are briefly reviewed.

It is suggested that the hazard of hepatitis and even fatality from pooled plasma is greater than that of a whole-blood transfusion from a single donor.

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# TYPHOID-BACILLUS INFECTION OF A SURGICAL WOUND TREATMENT WITH A URETHANE-SULFANILAMIDE MIXTURE\*

## Report of a Case

LOUIS WEINSTEIN, M D †

BOSTON

**A**LTHOUGH the occurrence of localized areas of suppuration caused by the typhoid bacillus is on the whole infrequent, McCrae<sup>1</sup> believes that during typhoid fever no part of the body in which abscesses may occur is exempt. *Eberthella typhosa* and pyogenic cocci, acting either alone or in combination, are the usual etiologic agents in this type of complication, which may occur without any apparent inciting cause, or as the result of injury to tissue by needle punctures, spontaneous hematomas or surgical procedures.

In most cases of abscess appearing in the course of typhoid fever, the lesions appear in various tissues without any apparent inciting cause. The buttocks are the most frequent site of abscess formation (McCrae<sup>1</sup>). Although localized areas of suppuration in the viscera are rare, spontaneously occurring abscesses of the thyroid gland, the cervical lymph nodes, the submaxillary glands, the breast (Sappington<sup>2</sup>), the spleen (Ransohoff and O'Rourke<sup>3</sup>), the ovary (Widal and Ravaut<sup>4</sup>), the rectus sheath (Bullowa<sup>5</sup>), the thigh muscles (Vires, Mas and Serre<sup>6</sup>), the muscles at the lower end of the sternum (Gannon<sup>7</sup>) and the peritoneal cavity, with or without perforation of the bowel, have been described. The reason for the focalization of typhoid bacilli in these various organs in typhoid fever in a particular patient is not apparent, but it seems most probable that during the stage of bacteremia organisms become located in these sites and, having established themselves, produce destruction of tissue.

Parenteral administration of various drugs has been incriminated in a number of cases as the cause for localization of typhoid bacilli in various muscles that have been used as sites of injection. Achard and Weil<sup>8</sup> have reported a case of abscess formation in muscle seven days after an injection of methylene blue in a patient with typhoid fever, aspirated pus yielded *E. typhosa* in pure culture. The intramuscular or subcutaneous administration of quinine (Schneider<sup>9</sup>), caffeine (Widal and Le Sourd<sup>10</sup> and Malenchini and Pieraccini<sup>11</sup>), oil of turpentine (Rathery and Bonnard<sup>12</sup>) and camphor (Tobias and D'Estefano<sup>13</sup>) has been reported as leading to formation of abscesses in some patients with typhoid fever, in most cases, the enteric organism causing

the primary disease was isolated in pure culture from the localized area of suppuration. Tobias,<sup>14</sup> who has recorded 2 cases of abscess formation due to the typhoid bacillus in typhoid-fever patients to whom camphor was administered parenterally, has expressed the opinion that such lesions when occurring during the acute course or convalescence of enteric fever are practically always due to *E. typhosa*. The pathogenesis of suppuration of this type appears to be mechanical irritation by the injected drug, with production of an area of decreased resistance and subsequent localization of organisms. Tobias could find no indication from his own cases or those reported in the literature that the appearance of an abscess has an unfavorable effect on typhoid fever, as a matter of fact, he expressed the opinion that in some cases the course of enteric fever is beneficially influenced by the development of a localized area of suppuration. Local injuries occurring without injections, such as hematomas in muscles, — which may result either from Zenker degeneration, which is sometimes present in typhoid fever, or from prolonged vomiting and coughing, affecting the abdominal muscles, — may serve to produce areas that are particularly susceptible to the establishment of the typhoid bacillus.

In spite of the fact that a moderate number of patients with typhoid fever develop complications requiring operative intervention, such as incision and drainage for osteomyelitis or laparotomy for intestinal hemorrhage or perforation, and that *E. typhosa* is capable of producing localized areas of infection, there is a scarcity of reports concerning suppurative complications of surgical wounds, a search of the literature having revealed only 2 such cases. Rathery and Bonnard<sup>12</sup> have described a case in which, following appendectomy because of pain in the right lower quadrant occurring at the onset of typhoid fever, the patient developed a superficial infection at the lower end of the operative wound, which, when incised and drained, yielded a pure culture of *E. typhosa*. A similar case of wound infection due to the typhoid bacillus following removal of the appendix in a patient who subsequently developed typhoid fever has been reported by Marta.<sup>15</sup>

The purpose of reporting the following case is to describe typhoid-bacillus infection in a surgical wound in the leg, without underlying osteomyelitis or periostitis, in a patient in whom the diagnosis

\*From the Haynes and Evans Memorials, Massachusetts Memorial Hospitals, and the Department of Medicine, Boston University School of Medicine.

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†Assistant professor of medicine, Boston University School of Medicine; visiting physician, Haynes Memorial, Massachusetts Memorial Hospitals.

f typhoid fever was first suspected on the basis of the bacteriologic findings in the local lesion, to point out the possible role of localized areas of suppuration in the spread of typhoid fever if, owing to lack of an exact bacteriologic diagnosis, proper precautionary measures are not taken, and to demonstrate the highly effective action of a mixture of urethane and sulfanilamide in the eradication of *E. typhosa* from a suppurated wound

M.C., a 68-year-old married woman, was transferred to the Haynes Memorial Hospital from the Orthopedic Service of the Massachusetts Memorial Hospitals to which she had been admitted on November 10, 1944, because of a fracture of the right femur sustained in a fall. She had enjoyed fairly good health until 3 weeks before admission to the Massachusetts Memorial Hospitals at which time she had a mild febrile illness characterized by generalized aching and a low degree of fever. A physician made a diagnosis of an upper respiratory infection and recommended bed rest for several days. Recovery occurred without any further treatment and the patient remained well until the fall which resulted in an intratrochanteric fracture of the right femur.

Open reduction was carried out on the day of admission and the bone ends were approximated by means of a Blount plate with complete closure of the wound. The course was uneventful until the 10th postoperative day, when there was a moderate elevation of temperature and the wound in the thigh appeared reddened, swollen and boggy and began to discharge purulent exudate. Cultures of the pus revealed *E. typhosa*. A macroscopic Widal test gave a positive reaction in a serum dilution of 1:320, both the organism isolated from the wound and a laboratory strain of the typhoid bacillus being used as antigens. Two subsequent cultures of the exudate from the wound taken during the next several days revealed the same organism. Because of these findings the patient was transferred to the Haynes Memorial Hospital on December 6 for further care and treatment.

At physical examination on admission the temperature was 104°F, the pulse 90, the respirations 20, and the blood pressure 125/75. The patient appeared much older than her stated age. She was moderately well developed and poorly nourished, appeared chronically ill and was unable to give an adequate history because of an extremely poor memory. There were no rose spots or petechiae or a rash of any kind on the skin. The mucous membranes were pale and moist and showed no abnormal pigmentation or hemorrhagic areas. The posterior cervical and axillary lymph nodes were palpable, small, of normal consistence and non-tender. There was no other lymphadenopathy. The pupils were equal in size and round and reacted to light and on accommodation. The scleras and conjunctivae were clear and of normal color. Examination of the eyegrounds revealed the disks to be of normal color, the margins well outlined and cupping of a normal degree. The retinal vessels showed narrowing, tortuosity and a moderate degree of arteriovenous nicking. No exudates or hemorrhages were seen. The right ear drum showed an old perforation, and the hearing was poor. The pharynx was clear and of normal color. The mouth showed no abnormalities except for absence of all but seven teeth, which were in poor condition. There was slight atrophy of the papillae of the tongue. The neck was not stiff, and there was no engorgement of the veins. The trachea was in the midline. The thyroid gland was not palpable. Examination of the chest revealed an increase in the anteroposterior diameter and equal expansion on both sides. Percussion over both lung fields was hyper-resonant, tactile and vocal fremitus were within normal limits and the breath sounds were clear except for a few dry rales at the right base. Examination of the heart revealed a diffuse impulse in the 5th left interspace at the midclavicular line, a regular rhythm, distant sounds and a rate of 90 per minute. There was a Grade II rough blowing systolic murmur heard best over the aortic area and transmitted down over the precordium. The pulmonic second sound was greater than the aortic.

The abdomen revealed no spasm, masses or tenderness. The liver was palpable 2 or 3 fingerbreadths below the right costal margin. The spleen and kidneys were not palpable.

No petechiae were noted on the abdominal wall. The genitalia were atrophic but revealed no other abnormalities. Examination of the extremities showed a well healed longitudinal scar 20 cm. in length on the lateral aspect of the right hip, in the center of this was a small sinus 1 cm. in depth from which drained a small amount of thin, grayish, foul-smelling exudate. Palpation of the scar revealed no tenderness or masses. The extremities were otherwise normal except for moderate pitting edema of both ankles. Neurologic examination showed the deep and superficial reflexes to be physiologic. No abnormal reflexes could be demonstrated.

A specimen of urine taken on admission had a specific gravity of 1.014 and contained no albumin, sugar or abnormal cellular elements. During the hospital stay, the specific gravity varied from 1.009 to 1.032, the albumin from 0 to ++, on one occasion and sugar was always absent. There were two episodes of pyuria, one in the 3rd and the other in the 7th week of the illness.

The red-cell count and hemoglobin were 3,910,000 and 10 gm. respectively, and remained at about these values during the hospital stay. The white-cell count was 6630 with 86 per cent neutrophils, 13 per cent lymphocytes, and 1 per cent eosinophils, and fluctuated thereafter between 4000 and 16,600 with essentially normal differential counts except on one occasion during the 2nd week, when 9 per cent eosinophils were present. The nonprotein nitrogen varied between 20 and 30 mg. per 100 cc. The serum calcium was 10.35 mg. per 100 cc. and the phosphorus 4.5 mg. The alkaline phosphatase level of the blood was 6 King-Armstrong units per 100 cc.

Cultures of the draining sinus in the right thigh made on admission revealed *E. typhosa* and a hemolytic *Staphylococcus aureus*. The gram-negative organism was again recovered 2 days later, but thereafter daily cultures of the wound, so long as it persisted, never again revealed the typhoid bacillus. On the 47th hospital day, 11 days after removal of the Blount plate, purulent exudate reappeared in the wound and bacteriologic studies revealed *Pseudomonas pyocyanea* in pure culture. This organism disappeared after 3 days of treatment. Further wound cultures were sterile.

Several cultures of the stool during the first 2 weeks in the hospital were negative for the typhoid bacillus, but in the 3rd week it was isolated. Five stool cultures made during the remaining 6 weeks were all positive for *E. typhosa*. Agglutinins against the typhoid bacillus, which had been present in a serum dilution of 1:320 on admission, rapidly increased, so that at the end of 2½ weeks they were detectable in a 1:1280 dilution.

X-ray examination of the chest revealed a few calcified mediastinal nodes and a network of increased density in both lungs, more marked on the right than on the left. There was no evidence of metastatic or primary neoplastic pulmonary disease. The right humerus showed an area of rarefaction made up of more or less round, pitlike areas measuring from 5 to 10 mm. in diameter, with sharply defined borders. Above this area was an amorphous calcification in the greater tuberosity. These findings were considered consistent with a small area of aseptic necrosis and were not thought to indicate neoplastic disease of the bone. Three roentgenologic examinations of the right femur at different times during the illness revealed no evidence of periostitis or osteomyelitis.

The temperature remained normal during the first 3 days in the hospital, fluctuated between 99 and 101°F for the next week and gradually declined to within normal limits for the remainder of the hospital stay.

The volume of the sinus in the right thigh as determined by the injection of sterile saline solution was about 30 cc. After the causative agent of the infection in the operative wound had been identified, injection of 15 cc. of a sterile aqueous solution of 10 per cent urethane and 1 per cent sulfanilamide<sup>15</sup> into the sinus every 4 hours throughout the day and night was begun. Under this regimen cultures of the wound for *E. typhosa* became negative in 36 hours and remained so during the remainder of the period of observation. The cavity decreased rapidly in size so that it was completely closed in 15 days. The quantity of urethane-sulfanilamide mixture injected daily was gradually diminished as the size of the sinus tract decreased, and treatment was stopped after 12 days.

On the 12th hospital day the patient complained of a sudden attack of intense, knife-like pain in the right hip, which was relieved by rest but markedly aggravated by even slight



motion of the leg. Examination revealed an area of tenderness on the lateral aspect of the right hip. Lateral rotation or flexion of the right hip joint produced severe pain. There was no change in the appearance of the wound, no masses or tenderness could be elicited, and no exudate was present. The temperature and white-cell count were within normal limits. Morphine sulfate was administered and sandbags were applied to the leg to immobilize it. X-ray examination of the right femur revealed penetration of the head of the femur by the blade of the Blount plate, the point of which was lying in the joint space. Subsequent treatment by the application of Buck's extension and sedation produced complete relief of pain in 3 days. Twenty-four days later, the healed wound in the leg was reopened and the plate was removed. At operation, the bone was found to be completely united, the muscles and fasciae were in good condition, and nowhere was there any evidence of infection. Cultures taken from various sites in the operated area were sterile.

On the 11th day after operation, the wound opened spontaneously and discharged purulent exudate, from which *Ps pyocyanea* was obtained in pure culture. The urethane-sulfanilamide mixture was applied every 4 hours to sterile dressings packed into the wound, and within 3 days the pigment-producing organism was absent, the purulent discharge ceased, and healing progressed so rapidly that the wound was completely closed 10 days after treatment was begun.

The hospital course was complicated by two episodes of pyuria, one in the 2nd hospital week and the other in the 7th. Bacteriologic study of the urine during the first bout revealed a pure culture of *E typhosa*. Several subsequent urine cultures were sterile until the second attack of pyuria, at which time a pure culture of *Ps pyocyanea* was isolated. Treatment with 2 gm. of sulfathiazole a day produced clearing of the urine in a short time.

Since the patient had become a typhoid carrier and required constant nursing attention because of her poor mental status, she was transferred to another hospital.

### DISCUSSION

There are several aspects of this case that merit detailed discussion. The original illness three weeks before fracture of the femur was in all probability an episode of extremely mild typhoid fever, which at its inception was mistaken for an upper respiratory infection, no effort being made to isolate the patient. Although the presence of *E typhosa* in the urine and stool could well have been due to the carrier state, the rapidly rising agglutinin titer indicates active infection. Had the patient not incurred a fracture of the hip, with subsequent infection of the operative wound by the typhoid bacillus, the diagnosis of typhoid fever would in all probability never have been made.

The manner in which the enteric pathogenic bacteria gained entrance to the wound is open to conjecture. It seems probable that the organisms were not brought to the site of operation by the blood stream, since, if it is assumed that the original illness three weeks previously was typhoid fever, the bacteremic stage should have been over for an appreciable time. In the third week of typhoid fever, it is usual to find the organisms either in the stool or the urine or in both, and it seems most probable that the wound infection took place as a result of the introduction of organisms during or after operation through the skin of the thigh, which was contaminated either with fecal material or with urine. That the organisms did not enter the wound as a result of infection of the under-

lying bone or periosteum seems likely, since no roentgenographic evidence of osteomyelitis or periostitis was obtained. That there was a typhoid bacillus abscess in the thigh muscles that was entered at the time of operation seems unlikely, since suppuration did not appear in the wound until ten days after surgical intervention. A remote possibility is that the organisms were present in the bone marrow without producing signs of osteomyelitis and were introduced into the wound during the procedure of inserting the Blount plate.

The similarity of the urine and wound cultures during the episodes of pyuria is of interest. When the wound was infected with *E typhosa*, the same organism was isolated in the urine culture, and since there was marked pyuria, it seems proper to assume that the patient at that time had an acute pyelonephritis due to the typhoid bacillus. When, following the second operation, the wound became infected with *Ps pyocyanea* and pyuria recurred, this organism was also cultured from the urine. These findings add some evidence in support of the possibility that infection of the wound resulted from contamination with bacteria that were present in the urine or the stool.

It has previously been demonstrated that *E typhosa* is extremely susceptible to the action of urethane, large numbers of these bacteria being killed in the test tube by an exposure of five to ten minutes to a 10 per cent concentration of this drug in broth.<sup>16</sup> The bactericidal effect also appears to be exerted in vivo, since treatment of the wound described above with a mixture of 10 per cent urethane and 1 per cent sulfanilamide resulted in complete sterilization within thirty-six hours. *Ps pyocyanea* has also been found to be highly susceptible to the action of urethane in vitro,<sup>16</sup> and this effect is apparently unaltered by the presence of a tissue or exudate. This drug seems worthy of a trial in any localized infection with the typhoid bacillus, *Ps pyocyanea* or other gram-negative organisms. It seems unlikely that the sulfanilamide in the mixture had any appreciable effect, since it is well recognized that the sulfonamides are relatively inefficient against gram-negative bacilli.

The danger of failure to recognize the presence of the typhoid bacillus in localized areas of suppuration should be stressed. If the diagnosis of typhoid fever is missed, as it may well be in extremely mild cases, such infected areas, which may be discharging a purulent exudate laden with *E typhosa*, may be responsible for the transmission of the disease to other persons because of lack of proper precautionary measures. As a matter of fact, a patient who was in the ward at the same time as the one described above became ill with severe typhoid fever and, so far as could be ascertained, the case reported was the source of the infection. Rubenstein<sup>17, 18</sup> has stressed the importance of unrecognized typhoid bacillus infection

n patients with acute or chronic cholecystitis who undergo surgical treatment as a source of spread of typhoid fever

The possibility that wounds occurring during the course of typhoid fever, either accidentally or as the result of various therapeutic procedures, will become infected with the typhoid bacillus must always be kept in mind by those treating this disease. The possibility that these secondary lesions will act as sources for the spread of infection to susceptible persons must be carefully considered in the establishment of proper isolation technic. The rarity of reports of secondary infections of wounds with *E. typhosa* in patients who are operated on for the intestinal complications of typhoid fever is quite surprising, and it must be assumed that, on the whole, the resistance of skin and muscle to infection by the typhoid bacillus is high. A careful bacteriologic examination of all local areas of suppuration occurring in the course of typhoid fever is imperative.

#### SUMMARY

A case of infection of a surgical wound with *Eberthella typhosa* in a patient who probably had an undetected mild attack of typhoid fever several weeks prior to operation for the open reduction of a fracture of the femur is described.

Treatment of the local infection with a solution containing 10 per cent urethane and 1 per cent sulfanilamide led to rapid eradication of the infecting bacteria and healing of the wound.

The importance of localized areas of suppuration due to *E. typhosa* cannot be overemphasized because, unless promptly recognized bacteriologically and the necessary precautions taken, spread of typhoid fever may occur.

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## SYMPOSIUM ON MEDICAL SOCIOLOGY

## MEDICAL PRACTICE AND ITS FUTURE\*

LELAND S. MCKITTRICK, M.D.†

I UNDERSTAND that my place in this symposium is to tell you something of medical practice as it is today and something of its past, and to speak of those forces within and outside of medicine whose influences point toward the medical practice of tomorrow.

You are approaching the end of your medical-school training. Except for minor digressions, your thoughts and efforts have been on the scientific aspect of your chosen profession. What you may know of the actual practice of this profession cannot have come from personal experience.

Clinical medicine is not a science. It is the utilization of what we have learned from study and experience to determine and interpret the variable physiologic and anatomic responses of the body and mind to external or internal stimuli, and the application of this knowledge in such a manner that the proper treatment will be prescribed and will be accepted and carried out by the patient and his family.

## THE DOCTOR

The practicing physician is the infantryman of the medical profession. To understand the practice of medicine, one must understand him, and this is not easy — especially for the nonprofessional person.

What are some of the outstanding characteristics of a good physician? A well developed intellectual curiosity, complete honesty, both moral and intellectual, and a devotion to his work that makes him available at all times of every day are some of the qualities that you have a right to expect in your doctor.

What are the factors that tend to develop and maintain in the physician the qualities that are so essential to good medical care of a community? I am not at all sure that I know the whole answer, but I believe that I do know at least a part of it. There are well recognized minimal requirements that medical schools must fulfill to give their students the minimum training essential to an adequate background for the practice of medicine. Schools that do not fulfill these requirements but accept medical students for training are of themselves inherently dishonest, and therefore cannot be ex-

pected to develop honesty in their students. A good school, a careful selection of students and the elimination of these found to be intellectually or morally unfit are, then, the first essentials.

The development of the proper emotional background of the doctor extends over a period of many years. Stimulated in the medical school, the young doctor has his most intensive exposure to the professional mind during his internship and in his association with the older men in the earlier stages of his entry into the actual practice of medicine. The practice in our teaching hospitals of holding staff meetings in which deaths, complications and errors are openly and frankly discussed exposes the young mind to a form of intellectual honesty not previously encountered. I thrill with pride each time one of our hospital residents voluntarily presents before the medical students and the staff a patient in whose management he has erred. By this action, he has accepted one of the basic principles of intellectual honesty, he has kept faith with himself, and has done what he could to prevent others from committing the same mistake.

Competition, both economic and professional, is an important and a most powerful influence. The practice of medicine to most doctors is their chosen way of making a living, and conversely, most doctors are dependent on their professional income for a livelihood. Every doctor knows that a satisfied and grateful patient is his greatest asset. You are rightfully told that if you can be a better doctor than your neighbor, are honest in your dealings with patients and are solicitous of their best interests, mentally and physically, you can be assured of a loyal and increasing group of patients and of satisfactory financial returns.

Every physician knows only too well of the patient's inability to distinguish what is good in medicine or surgery from what is bad. He knows, too, that there is no legislation or regulation that can adequately control the quality of medical or surgical care, except such regulations as are made by his professional associates. As a doctor, then, he not only has to satisfy the demands of his patients, but he must constantly strive to avoid any action that may receive the criticism of those professional associates, young or old, whose judgments he respects.

We hear much of the stimulus to do better work because of the personal relation between the doctor and the patient, and of the importance of the free

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†Associate in surgery, Harvard Medical School, visiting surgeon, Massachusetts General Hospital.

hoice of a physician There are many variations in the quality of medical care, not only within the same wards of our hospitals but even among patients under the care of a given member of the staff We might not like to admit this, but if we are honest with ourselves, we shall realize that we are emotional human beings and that we respond to certain stimuli, just as do others who are differently trained Later on in your daily work you will see patients under varying conditions — patients in the hospital wards who are merely the hosts of a given disease, the patient who may be referred to, not as Mrs Jones, but "the woman in the corner bed with a cancer of the stomach" You will treat that patient's disease well Later in the day you may go to your office and see a young mother with a similar condition She tells you frankly that you operated on a relative or a friend of hers and that her doctor suggested the names of several surgeons, but that she came to you because she knew of you and wanted you to operate on her if an operation was necessary She expresses her confidence in you and her willingness to do whatever you advise, whenever you say it should be done, and she may well add, "I want to put myself completely in your hands" The quality of medical care that a given patient will receive from you as a doctor is dependent not only on your ability and experience but on the intensity with which you apply yourself to a given problem, and not infrequently it is this effort, over and above the average, that means the difference between life and death to the patient Theoretically, all patients should get from the same doctor the same detailed care Nevertheless, rightly or wrongly, the man who comes to you because he believes in you over and above anyone else is the patient who may well get from you that extra effort that represents the difference between the best you have to offer and just good medicine

You may well feel that I have given too much time to the role of the individual, but the medical service of any community can be only so good as the doctors who are giving it In any plan or discussion, therefore, that involves the relation between the doctor and society, there must be included a discussion of the quality of the service that is to be given, as well as the factors that influence its availability or its extension

#### THE STRUCTURE OF MEDICAL PRACTICE

Various possibilities await the young man who has had a good training in his chosen branch of medicine Time will only permit a limited discussion of the more significant of these

A relatively small group of extra able, intense young men, whose great interest is in the teaching and advancement of the science of medicine rather than in the care of the patient, will go directly into full-time positions in large teaching hospitals They will become the outstanding leaders in the medical

education of tomorrow On their shoulders will fall the responsibility for the scientific advancement of medicine and that of pointing the way to its clinical application The importance and responsibilities of the subclinical branches of medicine, such as bacteriology, pathology and radiology, are now well recognized and attract an increasing number of young graduates The great majority of young men and women, however, will go into clinical medicine, and for them there are a variety of opportunities Many will return to their own homes or will go to their chosen communities as assistants to experienced and successful practitioners This association is particularly valuable to the young surgeon

Affiliation with an organized group, contract work in industry or simply starting a solo practice from scratch are some of the more usual openings However interesting and instructive these first years may be, with but few exceptions they will not be productive from the financial point of view They are considered to have been well spent if they permit a scant living but permit a continued opportunity to learn and to become acquainted in the community in which one expects to continue practice

Probably the most difficult problem faces the young surgeon In recent years it has been quite generally accepted that a minimum of five years after graduation is necessary for his training By the end of this period he will have had an intensive exposure to surgical problems and will have become accomplished, although still relatively inexperienced in the performance of surgical operations and in the care of surgical patients The surgeon's confidence in himself, his ability to make decisions, and his technical skill, are rapidly lost, however, unless he can maintain a constant exposure to the problems of surgery and their solution

Patients and referring physicians are slow in putting their confidence in a young surgeon, even though well trained Moreover, the latter himself soon finds that whereas he has had an excellent training in the running of a surgical service and in the technical aspects of surgery, there are many practical problems involved in obtaining and maintaining the confidence of the patient, his family and the local physician that can be mastered only through experience under the conditions associated with the actual practice of surgery

During this transition period, how is the young surgeon to maintain his technical skill while he acquires these other essentials necessary to his success? This question is immediately answered for those fortunate enough to obtain an association with a successful, experienced surgeon or with a group of surgeons, but for those not so fortunate this represents one of the major problems facing postwar medicine, and the answer is not yet at hand

In summary, American medicine of today consists of fulltime research workers and teaching physicians, the fee-for-service doctors the organized

clinics, either under the fee-for-service system, best exemplified by the Mayo, Crile and Lahey clinics, or the contract-service system, as offered by the Ross-Loos Clinic, of Los Angeles, and contract work, including insurance practice, such as has been in force in many parts of this country for the past half-century. In addition there are the subclinical branches of medicine so essential to modern practice.

#### INFLUENCES WITHIN THE MEDICAL PROFESSION

Time will only permit the consideration of some of the more important forces within the profession that have influenced or are influencing medical practice in this country.

##### *The American Medical Association*

The American Medical Association was founded in 1847 "to promote the science and art of medicine and the betterment of public health." The *Journal of the American Medical Association* appeared in 1881, but neither it nor the Association was an active power in American medicine until the early part of the twentieth century. Membership is open to all legally registered physicians or graduates of qualified medical schools who have fulfilled the requirements of the local county medical society, in other words, membership in the latter automatically gives membership in the state and national organizations, with no additional dues or assessments for the latter. Members who subscribe to the official journal or one of its specialty journals become fellows of the Association. About 125,000 (approximately 70 per cent) of the physicians of this country are now members of the American Medical Association.

Although primarily educational in scope, the Association has a profound influence on medical practice. In recent years it has been much criticized for its conservatism, as expressed by its opposition to radical changes in the methods of medical practice. Although there is ample evidence that it has accepted certain changes, it is difficult to find anything to suggest an aggressive attitude on the part of the Association in favor of such changes, and it has violently opposed any alterations that are considered detrimental to the welfare of patients. There is, however, in the literature overwhelming evidence of its contribution to the advancement of the quality of medical education and medical care in this country. Only the briefest reference may be made to the more significant of these contributions.

In the early nineteen hundreds, through its Council on Medical Education and Hospitals, the Association was the most important single factor in setting and obtaining acceptance of the minimum standards of medical education and in eliminating a large number of so-called "diploma mills" and substandard medical schools. As a result of this, the number of medical schools in this country was

reduced from one hundred and sixty-six to seventy-seven.

The American Medical Association is the central figure in the most comprehensive and effective system known for the perpetuation and exchange of medical information and opinion. The *Journal of the American Medical Association* is probably the foremost medical journal of the world. In addition, the Association has created and supports journals in many of the specialties, as well as the *Quarterly Cumulative Index* and *Hygeia*, a magazine to the laity.

The educational value of the annual meeting of the Association, with its scientific exhibit, is outstanding. The councils on Pharmacy and Chemistry, Foods and Nutrition, and Physical Medicine and the many committees appointed from time to time, such as the Committee on Cosmetics, the Committee on Contraceptives, the Committee on American Health Resorts and various committees appointed by sections, have helped to correlate scientific knowledge and to promote rational thinking in their respective fields, as well as to demonstrate that honest advertising is not only a moral obligation but is also consistent with profitable and satisfying material progress.

The Association's relentless campaign against quackery is well known. According to *Fortune*, this has resulted in the American Medical Association's being threatened with suits totaling \$35,000,000 in the thirty years prior to 1938, of which only two ever came to trial, the total assessed damages amounting to just one cent.

It has fully co-operated with our government in the prosecution of the war, and is at present taking a leading part in plans for the guidance and post graduate education of returning medical officers after the war.

##### *Group Clinics*

*Fee-for-service system.* The late nineties and the early nineteen hundreds saw in Rochester, Minnesota, the beginning of what was to become the best known group clinic in the world. As the years passed, the Mayo Clinic, under the guidance of Dr. Will and Dr. Charles, became the center of the best in medicine and surgery, and one of the best in scientific research and the training of physicians. Subsequent to this, there arose a large number of similar but smaller groups, particularly throughout the Middle West. Of all the many clinics that have developed however, only three have reached national and international prominence. These are the Mayo Clinic, the Crile Clinic, of Cleveland, and the Lahey Clinic, of Boston. In addition to the excellence in the quality of medicine provided, these clinics have one common and apparently essential factor: the presence of an unusually able and dynamic leader — in each case a surgeon — who has excelled not only professionally but in the organization, selection and

he management of personnel necessary to the success of the undertaking

*Contract-service system* In 1929, Dr. Donald E. Ross and Dr. H. Clifford Loos, of Los Angeles, were approached by members of the Department of Water and Power of that city concerning the possibility of organizing for them a medical service, financed through periodic payments. With this stimulus, the Ross-Loos Clinic group was formed and began to function on April 1, 1929. For a monthly fee of \$1.50 — later raised to \$2.00 — for each subscriber, the group agreed to provide medical service, including attention either from a general practitioner or a specialist in the central offices or the hospital, or in the subscriber's home if the patient was unable to come to the clinic. Subscribers were to receive laboratory and x-ray services, physical therapy, ambulance service, drugs, dressings and hospitalization in a ward bed. Additional charges were made for certain services, such as dental work, special drugs and appliances.

In 1934, Dr. Ross and Dr. Loos were expelled from the Los Angeles County Medical Society not because the clinic was engaged in contract practice but because it was alleged that there was a solicitation of patients. The expulsion was sustained by the California Medical Association, which automatically brought suspension from the American Medical Association. According to the constitution of the latter, such expulsion is subject to appeal before the Judicial Council. This appeal was made, and on January 2, 1936, the action of the county and state societies was overruled. The conclusions reached by the Judicial Council were as follows:

a The appellants were brought to trial with no definite knowledge of what they were charged

b There was no adequate opportunity to defend themselves

c They were expelled for some unknown act not appearing in the charges

d They did not have a fair trial

Following this action by the Judicial Council, the two physicians were reinstated by the county medical society.

At the present writing there are one hundred and ten full-time doctors of medicine in the group, all of whom are members of the county medical society and therefore of the American Medical Association. Dr. Loos is a member of the House of Delegates of the California Medical Association and holds an important chairmanship in the local society; indeed, it is said that a most cordial relation exists between the physicians of the clinic and other doctors in the area. The clinic provides service for about 110,000 people in the Los Angeles area. The cost to the subscriber is \$2.50 a month. Dependents of subscribers are not included in this fee, but are accorded care at special rates — for example, office consultation or treatment, 75 cents, refraction, \$1.00, residence calls, daytimes, \$1.50, and nights (between 9:00

p.m. and 8:00 a.m.), \$2.00, minor operations, \$15.00, and major operations, \$25.00.

The above group and others similarly organized and controlled maintain excellent standards of medical service. Unfortunately, there developed in many communities groups supposedly organized on the same basis but actually organized by lay promoters, patronage being secured by advertising and solicitation. Where such organizations have developed, competition for patronage has resulted in a reduction of premiums and a lowering of the quality of medical care. In one state one hundred and forty-three such organizations were promoted as medical-service plans, with lay promoters acting as medical brokers and in some instances contracting with clinics or private groups of physicians in hospitals for the services promised to the prospective patient. In other groups no medical contracts were made and therefore no medical services were available to the enrolled members.

#### *Nonprofit Prepayment Hospital-Service and Medical-Service Plans (Blue Cross and Blue Shield)*

"Back in 1929, when Baylor had an idea that hospital costs could best be borne by group action, a budget plan for meeting certain but unpredictable hospital bills was established." This quotation is from a letter written in August, 1944, by Lawrence Paine, administrator of Baylor University Hospital of Dallas, Texas, and gives the beginning of what has become known as the Blue Cross program. Group Hospital Service, Incorporated, of Dallas, was inaugurated on a statewide basis in 1939 and experienced a phenomenal growth, but two years later was confronted with a deficit of \$110,000. Then followed a period of readjustment, and one year later Group Hospital Service was pronounced financially sound.

The Blue Cross program, as it has come to be known, was designed to cover the cost of hospitalization for patients in the lower-income groups who went into hospitals at so-called "semiprivate" accommodations. It covers either individuals or families, and usually includes all the ordinary costs payable to the hospital for a given period of time, generally three weeks. Persons must join in groups. The organization is on a nonprofit basis, and the cost for its protection is about 85 cents a month for an individual and \$2.00 for family membership. At the present time approximately 18,000,000 persons in this country subscribe to the program.

In addition to the Blue Cross program there are medical-service plans, most of them sponsored by the medical societies of various states. One of the largest and most successful of these is Michigan Medical Service, which was organized on a statewide basis by the Michigan State Medical Society in 1940. When first established, it gave, in conjunction with Michigan Hospital Service, complete hospital, medical and surgical services to subscribers

and their families. There is no income limitation on eligibility to enroll, but if the income of an unmarried subscriber is more than \$2000 or that of a married one is more than \$2500, the amounts allowed may not be adequate to cover the entire professional fee. In 1942, the Michigan Medical Service had to discontinue its medical coverage in favor of surgical coverage only. There is ample actuarial experience for the successful establishment of a surgical plan. The problems involved in sound actuarial medical plans have, however, not yet been satisfactorily solved, although all plans look forward to the inclusion of medical services as increasing experience permits. To us in Massachusetts, it is encouraging to learn that in the first quarter of 1945 the Massachusetts Medical Service — established by the Massachusetts Medical Society — had the largest net enrollment of any medical society plan in the country, and that in the near future it anticipates the inclusion of medical care in the hospital without an increase in rates.

In addition to the Blue Cross and Blue Shield programs, a large number of projects under the stimulus and guidance of medical groups are being put into practice throughout the country. Thus, the State Medical Society of Wisconsin is actively working at the present time on a plan to provide complete coverage to low-income groups throughout the entire state.

### *Medical Committees*

*The Committee of Physicians for the Improvement of Medical Care, Incorporated.* This committee was formed in 1937 by a small but well known group of physicians, many of them in the field of medical education. They believe that "the health of the people is a direct concern of the Government." This committee has taken an active part in an attempt to outline the principles of an improved medical practice. Its communications have been few but dignified and constructive, although many times not in agreement with current medical thought. Its letter of congratulation to Senator Wagner after the introduction of his bill (S 1161) suggests that the committee was willing at that time to favor the adoption of a compulsory federal health system.

*The National Physicians Committee for the Extension of Medical Service.* This committee was established in 1939. Most if not all of its members, too, are well known in medical circles, although they are more representative of medical practice than of medical education. This committee has no direct affiliation or working connection with the American Medical Association, but its principles have been endorsed by the House of Delegates of the Association and active in its work are some who are or have been actively interested in the American Medical Association. The National Physicians Committee believes that the necessary and desirable steps to improve and spread the cost of medical

care can best be done within the framework of principles approved by the medical profession. It favors state and local rather than federal subsidies to the indigent. The committee has been criticized for its violent attack on the Murray-Wagner Dingell Bill. Its widely heralded opposition to S 1161 and the committee-sponsored polls by the Opinion Research Corporation, of Princeton, New Jersey, have, however, undoubtedly done much to awaken the medical profession of the country to the need of taking an active part in developing or recognizing an improved medical practice more acceptable to the public who pays for it.

### INFLUENCES OUTSIDE THE MEDICAL PROFESSION

#### *Group Insurance for Industrial Workers*

In 1912, Montgomery Ward and Company, of Chicago, purchased from an insurance company a group-insurance policy. This provided life insurance for all employees and is said to be the first group life-insurance policy written by any private carrier in this country.

For over twenty-five years, the Endicott-Johnson Shoe Company, of Binghamton, New York, has provided full medical care and hospitalization for all workers and their dependents, without cost. Between that time and the present, there has developed an increasing interest on the part of industry in the type of medical care given to employees and their dependents, and in 1943, according to a recent survey of the National Physicians Committee, there was a total of nonduplicated insurance — including the Blue Cross — in this country covering more than 25,000,000 persons. The coverage in the various policies varies tremendously, as does the proportion of the cost paid by the worker and by the employer. It has been suggested that complete group health insurance might consist of the following for employees, life insurance, equal to approximate annual earnings, sickness benefits equal to 25 to 50 per cent of the weekly wage, hospitalization from \$4 to \$7 a day, hospital extras from \$20 to \$35 for each illness, surgical care on the basis of a fee schedule (maximum, \$150), medical care with a fixed maximum benefit and a retirement annuity based on service earnings, and for dependents, identical coverage for hospitalization and surgical and medical care.

There are, however, definite weaknesses in each of the group policies now available through private companies. Outstanding among these weaknesses are the facts that too large a group is required to obtain minimum costs and that insurance protection may be forfeited when employment ceases.

Outstanding in its accomplishments is the highly successful prepaid medical plan that has been set up by Dr. Sidney Garfield at the direction of Mr. Kaiser for his shipbuilders in California (Southern Permanente Foundation) and Washington (North-

n Permanente Foundation) In the Oakland California plant 62,000 of the workers (90 per cent) have joined the plan which is voluntary. Excellent and complete care is given in their own hospitals because of war-time limitations the families of the workers are not included. The organization works in complete harmony with the local medical profession.

#### *Group Health Association, Incorporated*

This association was granted a charter in Washington, D. C., in February 1937, with an appropriation of \$40,000 from the Home Owners' Loan Corporation. Through a staff of hired physicians, it proposed to offer to federal employees and their families most types of medical and surgical care at a stated annual cost. The Medical Society of the District of Columbia opposed this scheme believing that it was not to the best interests of the public or the physician and was in violation of its code of ethics. According to an article that appeared in the *Journal of the American Medical Association* just before the Group Health Association began to function actively, it was thought that the organization was practicing medicine illegally and that the physicians employed were primarily the agents of the association and not those of the patients and that since the bylaws provide that the medical director shall render such reports as the Board of Trustees shall require, all privacy and secrecy between physician and patients would be destroyed. It was also held that there was no opportunity for the freedom of choice of his physician by the patient. One of the members of the Medical Society of the District of Columbia was therefore expelled, and several other physicians resigned from the association. Following this, the American Medical Association and others were indicted by the Department of Justice and were convicted of violating the Sherman Anti-Trust Act. This conviction was upheld by the United States Supreme Court.

#### PROPOSED CHANGES

##### *Murray-Wagner-Dingell Bill*

On June 3, 1943, Senator Wagner — for himself and Senator Murray — presented a bill (S 1161) framed to broaden the present Social Security Act. It included a provision for medical care supported through payroll deductions for the employed and direct taxation for the self-employed.

According to the committee appointed by the American Bar Association to study and report on this bill, its authors are Isadore S. Falk and Wilbur J. Cohen, director and assistant director, respectively of the Bureau of Research and Statistics of the Social Security Board, and Philip Levy, secretary to Senator Wagner. It may therefore be assumed to represent the opinion of the Social Security group concerning the manner in which the health of the people can be best protected. It provides

complete medical and hospital care for approximately 110,000,000 persons. It provides for an advisory health council to be appointed by the Surgeon General of the United States Public Health Service whose members are authorized to advise him with reference to carrying out the provisions of the act. It provides aid for research and for undergraduate and postgraduate education. It puts complete responsibility for carrying out its provisions on the Surgeon General.

The bill met with violent opposition from many quarters — the American Medical Association, the National Physicians Committee, the American Bar Association, most business organizations and many others who saw in it the centralization of medicine as the initial step toward more complete centralization of all American activities. Organized labor, the National Farmers Union and most social workers favored its passage. It has not been and probably will not be reported from committee.

##### *Pepper Committee Report*

The Senate Subcommittee on Wartime Health and Education, with Senator Claude Pepper as chairman, has recently reported on the investigation by this committee of the health of the Nation. It emphasizes that its findings are preliminary. It recommends that federal grants-in-aid be made to the states for the construction of hospitals, medical centers and health centers in accordance with integrated states' plans approved by the United States Public Health Service. It reports an acute shortage of personnel with training in psychology and psychiatry and points out the need of increasing such personnel. It recommends that federal scholarships or loans be made available to qualified students, and urges an increased enrollment of women in medicine, dentistry and so forth. It makes no specific recommendations in regard to health insurance, but points out the importance of group financing. The report states:

Any method which is evolved should offer complete medical care, should be reasonably but not "cut rate" in cost, should include substantially all of the people, should afford the highest quality of care, should permit free choice of physicians or groups of physicians, should allow democratic participation in policy making by consumer and producers, should be adaptable to local conditions and needs, and should provide for continuous experimentation and improvement.

The report is well written and suggests that the work and recommendations of this committee should be carefully followed by all those interested in the future of medical practice.

\* \* \*

In closing, let me remind you that the practice of medicine as you will know it may differ in many ways from that which we know today. There are many forces at work both within and outside medicine to give all the people of this country the best possible medical care at a cost within their





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the conditions under which he practices, and the opportunities and incentives for continued educational advancement, and that any changes in medical practice that do not have as their primary objective a continued improvement in the quality of service given may well lower rather than elevate the standard of health of the American people

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

#### CASE 32061

##### PRESENTATION OF CASE

A fifty-year-old theater manager entered the hospital complaining of vomiting of blood.

Five months before admission he felt nauseated and vomited a large blood clot. After this episode he felt well until six weeks later, when he again experienced severe nausea and vomited a large quantity of blood. During the following three days he had four more massive hematemeses, with tarry stools. He had received several blood transfusions.

The past history revealed that for years the patient had complained of upper abdominal pain, gaseous eructations and nausea. At the age of thirty-five an exploratory laparotomy because of continued discomfort revealed a "bulbous growth on the appendix," and an appendectomy was performed. Twelve years before admission the patient had five pleural effusions in one year and was sent to a sanatorium for eleven months. For about one and a half years after discharge he had no pain. Ten years before admission, attacks of severe epigastric pain, nausea and flatulence began. They were not related to meals, frequently occurring at night. The pain usually began in the right costovertebral angle but then spread anteriorly over the right upper quadrant, with some radiation across the left side and toward the back. The pain was not relieved by alkalis or a bland diet but was always relieved by vomiting. Two years before admission a gastric aspiration revealed acid-fast bacilli. He again went to a sanatorium, where the sputum and gastric juice were each positive on one occasion. During the fifteen months before admission the gastric juice was negative for acid-fast bacilli.

Physical examination revealed the patient to be well developed and nourished and in no distress. The heart, lungs and abdomen were normal.

The temperature was 97.4°F, the pulse 82, and the respirations 18. The blood pressure was 108/81 systolic, 70 diastolic.

The red-cell count was 4,860,000, with 14.3 gm. of hemoglobin. The white-cell count was 12,700. The urine was normal, as were the blood chemical findings. Gastric analysis revealed 5 units of free hydrochloric acid in the first specimen, 15 units in the second and 79 units in the third. The gastric juice was guaiac negative and contained no acid-fast bacilli by the alum flocculation method.

A gastrointestinal series showed no evidence of esophageal varices or of hiatus hernia. The stomach was normal in form and function. Barium passed the pylorus without delay, filling the duodenal bulb to a normal contour. The tip of the bulb, however, was consistently deformed, especially when the bulb was collapsed. A definite ulcer crater could not be found. Barium passed rapidly through the small bowel. A barium enema was essentially negative.

An operation was performed.

##### DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: Before seeing the x-ray films we might summarize this story. This man began to bleed five months before admission, vomiting a little blood. Six weeks later he had recurrent, apparently massive, hemorrhages over a period of three days. He vomited blood, and he passed bloody stools. He had several blood transfusions. Although it does not so state, I presume that it is fair to assume that he had had no bleeding for approximately three and a half months. In the past he had had a good deal of abdominal pain, which to me is indefinite in character and means nothing so far as pointing to a diagnosis is concerned. It was not characteristic of a duodenal ulcer or of gallstones, indeed, it was not characteristic of anything and means nothing to me at the moment. This man had acid-fast bacilli in the sputum. I presume that tuberculosis alone would not be adequate for a diagnosis. I do not believe, however, that we should spend more time on it, it probably does not enter into our problem, since we do not have to decide whether the patient should be operated on. I think we can safely assume that the blood came from the upper gastrointestinal tract and not from the bronchial tree.

DR MILFORD D SCHULZ Then I shall just tuck this x-ray film of the chest down in the corner

DR MCKITTRICK I am constantly looking with great expectation to the day when the radiologist helps me at this stage of the game

DR SCHULZ I do not believe that this is the time these are the films of the colon, made on two successive days. The second examination was made because of a defect seen near the splenic flexure. It is no longer evident on the second examination. These are films of the lower esophagus and they show no evidence of varices. The stomach is quite normal in appearance. The only thing seen is the deformity of the distal portion of the duodenal bulb, but there is no evidence of an active ulcer crater. The duodenal loop is entirely normal in appearance. There is nothing abnormal in the appearance of the small bowel.

DR MCKITTRICK Thank you, sir. I continue to appreciate your efforts.

I might say right now that I am not going to make a diagnosis because I do not know what this man had. The blood that he vomited probably came from the stomach or duodenum. I say that simply because we have no evidence that it could have come from any place else. There were no symptoms or evidence suggestive of anything in the esophagus; he did not have varices demonstrable by x-ray, and no hiatus hernia. Without symptoms referable to the esophagus and without evidence of a lesion of the esophagus by x-ray, the esophagus is out of the picture so far as I am concerned. We know that the blood could not have come from a site much lower than the duodenum because most of it was vomited. Therefore, we are not concerned with anything below the level of the duodenum. That narrows the field to the stomach and the duodenum, and there is something more than the fact that this is a conference case that makes me suspicious that what the x-ray films show was not the cause of this man's bleeding. This is only a suspicion because there is nothing definite to go on.

The patient had vomited blood with blood clots on one occasion. Possibly that is more suggestive of the stomach than the duodenum, but I am not sure of it. I completely distrust his story so far as it has anything to do with the present situation. The bleeding might have been due to a duodenal ulcer, or it might not. There is, as you know, a lesion sometimes called duodenal ulcer occulta, an ulcer in the second portion of the duodenum in the region of the ampulla. The symptoms in such cases are indefinite, the patient may be operated on for almost anything except duodenal ulcer, and the ulcer is apt to be missed at operation unless the surgeon is particularly on the alert. This may be one of these cases, but I doubt it. We do not have the benefit of x-ray examination promptly after the hemorrhage. Careful x-ray study at such a time is particularly useful.

It has been my very limited experience that when I am not able definitely to demonstrate from the clinical evidence the source of a man's bleeding I am apt to be disappointed at operation. A gastroscopy was not done. I do not know of any reason why it should have been done. I presume that if this man had active gastritis it probably would have shown by x-ray examination although all the acute episodes happened three and a half months before entry. Since I have to make a diagnosis, I shall have to call the lesion a duodenal ulcer because of the deformity shown at x-ray examination, but I shall quickly add that this is probably wrong. I am strongly suspicious that the bleeding came from the stomach. If it came from the stomach it could have been caused by any one of a number of things including an ulcer or gastritis that had healed. I believe it was likelier due to a lesion that was missed by x-ray examination. Even the X-ray Department does occasionally miss a definite lesion of the stomach. I do not believe however, that it often misses an ulcer or a carcinoma, but something like a leiomyoma is sometimes difficult to spot particularly if it is small. I have to leave it at that.

I will say that this man had a healed duodenal ulcer but I am suspicious that tucked away in the stomach some place there was a lesion from which this man bled.

DR TRACY B MALLORY Are there any other suggestions?

A PHYSICIAN Was this man an alcoholic?

DR GORDON A DONALDSON No.

DR MALLORY Will you tell us about the operative findings, Dr Donaldson?

DR DONALDSON We were just as unhappy about the diagnosis as Dr McKittrick is. There were many points in favor of a duodenal ulcer. We thought that the bleeding was typical of the upper gastrointestinal tract and this patient was a perfect type for an ulcer since he was a thin asthenic, theatrical manager, with a high gastric acidity.

We were also interested in the upper abdominal cramps, which he had had for years, and at operation, Dr Allen carefully explored the ileocecal region. The vessels over the serosa were definitely dilated, but the bowel wall seemed to be essentially normal. We thought that the bleeding could not have come from that source. There was an avascular adhesion between the gall bladder and the duodenum, which was cut, and the duodenum was thoroughly explored without finding any evidence of induration or ulceration. He then turned his attention to the stomach itself, and while he was exploring the mesenteric border, high on the lesser curvature the cause of the bleeding was found.

#### CLINICAL DIAGNOSIS

Duodenal ulcer

DR MCKITTRICK'S DIAGNOSIS

Duodenal ulcer

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Physical examination revealed the patient to be well developed and nourished and in no distress. The heart, lungs and abdomen were normal.

The temperature was 97.4°F, the pulse 82, and the respirations 18. The blood pressure was 108 systolic, 70 diastolic.

The red-cell count was 4,860,000, with 14.3 gm. of hemoglobin. The white-cell count was 12,700. The urine was normal, as were the blood chemical findings. Gastric analysis revealed 5 units of free hydrochloric acid in the first specimen, 15 units in the second and 79 units in the third. The gastric juice was guaiac negative and contained no acid-fast bacilli by the alum flocculation method.

A gastrointestinal series showed no evidence of esophageal varices or of hiatus hernia. The stomach was normal in form and function. Barium passed the pylorus without delay, filling the duodenal bulb to a normal contour. The tip of the bulb, however, was consistently deformed, especially when the bulb was collapsed. A definite ulcer crater could not be found. Barium passed rapidly through the small bowel. A barium enema was essentially negative.

An operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: Before seeing the x-ray films we might summarize this story. This man began to bleed five months before admission, vomiting a little blood. Six weeks later he had recurrent, apparently massive, hemorrhages over a period of three days. He vomited blood, and he passed bloody stools. He had several blood transfusions. Although it does not so state, I presume that it is fair to assume that he had had no bleeding for approximately three and a half months. In the past he had had a good deal of abdominal pain, which to me is indefinite in character and means nothing so far as pointing to a diagnosis is concerned. It was not characteristic of a duodenal ulcer or of gallstones, indeed, it was not characteristic of anything and means nothing to me at the moment. This man had acid-fast bacilli in the sputum. I presume that tuberculosis alone would not be adequate for a diagnosis. I do not believe, however, that we should spend more time on it, it probably does not enter into our problem, since we do not have to decide whether the patient should be operated on. I think we can safely assume that the blood came from the upper gastrointestinal tract and not from the bronchial tree.

series of films I have a few questions that I should like to ask him. I have not seen the films.

DR CLAYTON H. HALE: Unfortunately the films were all taken with the patient in bed and are not entirely satisfactory. We have here a heart that is somewhat enlarged, especially in the region of the ventricles. The aorta is tortuous, and there is a suggestion in one of the films that the ascending aorta is slightly widened.

DR BLAND: Three sets of films are described. I am particularly interested in the one taken on admission.

DR HALE: In the first film there is a rather hazy area of density in the left lower lobe and a fairly tortuous aorta. The right hilum is more prominent than the left. I do not believe that we have ever made a preautopsy diagnosis of massive pulmonary embolus by x-ray examination, although a review of the films of some of these cases has suggested that the involved pulmonary artery was larger than normal. We cannot make such a diagnosis from these films, but one would have to think of it as a possibility. The shadow in the lungs is not typical of an infarct. On the lateral film taken two days later you can again see an area of density, but this also does not look like an infarct. It looks more like an area of atelectasis in the lower lobe. The costophrenic sinus is slightly obscured, possibly by a small amount of fluid.

Another diagnosis that we have trouble in making by x-ray examination is dissecting aneurysm of the aorta. Looking back over the films of some of these cases, after the diagnosis has been proved, has suggested to us that the loss of definition of the descending aorta in the lateral projection may be a significant sign in making a diagnosis of dissecting aneurysm of the aorta. On the lateral chest films of this case the descending aorta is not clearly seen, but these are not good films, so that I do not know how much we should depend on the sign in this case.

To sum up what I have said, this man had a large heart, with no evidence of pulmonary edema. I see no characteristic shadows of infarcts. I interpret the shadow in the lower lobe as consistent with atelectasis, and the ascending aorta looks widened. This undoubtedly was a sclerotic aorta. The significance of the prominent right pulmonary artery is questionable. The absence of sharp definition of the aortic shadow below this point in the descending aorta must make one think of the possibility of a dissecting aneurysm, but one cannot safely make this diagnosis because of the poor quality of the available films.

DR BLAND: Do you want to comment on this streak in the left upper chest?

DR HALE: I should think that it was a small area of atelectasis.

DR BLAND: Could it represent a healed infarct?

DR HALE: It could, but its shape and location are rather unusual for an infarct.

DR BLAND: In looking back over the history, it is clear that this patient had phlebitis. He had swelling of one leg and pain in the other, so that it must have been a fairly extensive process. I suspect that he had had phlebitis longer than the record indicates, indeed that he had it before he came into the hospital. That is somewhat supported, I think, by the scar in the lung, which looks to me as if it could easily be one of the scars that Dr. Castleman and Dr. Hampton have so well described. He had, in addition to the phlebitis, clinical evidence of pulmonary emboli. The onset of his illness qualifies well. Its abruptness is mildly against coronary thrombosis and much more in favor of a large pulmonary embolus or a dissection of the aorta. The fact that the electrocardiogram, except for the irritability of the heart, was essentially normal should not disturb us too much in the diagnosis of pulmonary embolus.

DR BENJAMIN CASTLEMAN: Two more electrocardiograms were taken that are not recorded in the clinical abstract.

DR BLAND: As I look at them quickly I should say that they are essentially normal. There is no prominence of the S waves in Lead I or of the Q waves in Lead 3, which sometimes occurs during the first few hours after a large embolus. There is no inversion of the T waves in Lead 3, and no tendency to right-axis deviation. It should be remembered, however, that only about 10 per cent of patients with pulmonary embolus get acute cor pulmonale and that we believe the electrocardiogram is simply a reflection of the acute dilatation of the right side of the heart. It is evidence of considerable weight against coronary thrombosis, and it helps us only in a negative fashion in our consideration of possible dissection of the aorta.

When we examine the recorded findings in the heart for evidence of acute cor pulmonale, in addition to the electrocardiogram, the usual things that we look for are not commented on — namely, accentuation of the pulmonic second sound, and gallop rhythm — and certain murmurs that we should not expect to find in this condition are mentioned. Tachycardia and irritability of the heart are quite frequent with pulmonary emboli. Usually it is ventricular irritability that predominates. Therefore, we must conclude that there is nothing in the heart on first examination to indicate acute right-sided dilatation. The patient's subsequent course, however, indicates that he must have had pulmonary emboli and infarction. The transient changes described in the x-ray films seem to fit in very well with Dr. Hampton and Dr. Castleman's description of incomplete infarction of the lung, in which the shadows clear up quickly, thus indicating functional infarction without actual destruction of the pulmonary tissue. Then, of course, the

## ANATOMICAL DIAGNOSIS

## Neurinoma of stomach

## PATHOLOGICAL DISCUSSION

DR MALLORY This was a tumor of the stomach wall. It projected only externally from the muscle layer, which explains the failure of the X-ray Department to visualize it. There was a slight crater—a shallow ulceration of the mucosa just over the tumor. If that had been caught in a certain plane, it might have been demonstrable.

The tumor was of the spindle-cell type, which pathologists usually argue about—whether it is a leiomyoma or tumor of nerve-sheath origin. We classified this as a neurinoma, which is, in my opinion, the more frequent of the two tumors in the stomach. It was slowly growing and can safely be called benign. There is not much doubt that the man is cured.

## CASE 32062

## PRESENTATION OF CASE

A fifty-year-old pipefitter was admitted to the hospital complaining of substernal pain.

One hour before admission he was doing his regular work at the Navy Yard but exerting himself more than usual. He was suddenly overcome by a sensation of heavy substernal compression. He felt weak and sat down. He was taken to the Infirmary, where he was given 16 mg of morphine sulfate. He was then brought to the Emergency Ward, where he complained of substernal pain radiating to both scapulas.

The past history revealed that a year before admission the patient was treated at another hospital for olecranon bursitis. At that time the blood pressure was not recorded. The heart was not enlarged, and the pulse was 70 and regular. There were no cardiac murmurs. A Kahn test was negative. Twelve years before admission he was found to have a systolic blood pressure of 185, which decreased after treatment. Eighteen years before admission he was treated for a urethral stricture, but he denied venereal disease. At no time had there been any evidence of cardiac failure.

Physical examination revealed the patient to be apprehensive and pale. He was not dyspneic. The skin was moist. The heart was enlarged to the left, but the border was difficult to percuss. Extrasystoles were frequent, with occasional runs of eight or more. A Grade I systolic murmur and a Grade II diastolic murmur were heard at the apex. At the base, over the sternum, was heard a Grade III to-and-fro murmur, loudest in diastole. There were no thrills, and no carotid transmission. The lungs and abdomen were normal. There was no ankle edema.

The temperature was 98°F, the pulse 84, and the respirations 20. The blood pressure was 160 systolic, 100 diastolic.

The red-cell count was 5,300,000, with 14.5 gm of hemoglobin. The white-cell count was 13,400, with 87 per cent neutrophils. The urine gave a ++ test for albumin, and the sediment contained an occasional white cell.

An x-ray film of the chest taken on the first hospital day showed an area of increased density lateral to the apex of the heart and in the cardiophrenic angle. Above this, at the level of the left hilus, there was a linear shadow of increased density. The aorta was rather tortuous. Another film, taken on the second hospital day, showed a similar picture, with a small area of hazy density at the left base. A third film, taken on the day before death, showed that this area had almost completely disappeared. An electrocardiogram showed normal rhythm, with a rate of 100. Evidence of left axis deviation was present. The PR interval was 0.15 second. There were many premature beats in Leads 1 to 2 that originated from varying ventricular foci. The T waves were upright in Leads 1 and 2 and in the precordial lead but flat in Lead 3. QRS was slurred. There was a run of ventricular tachycardia in CF.

Soon after admission 0.2 gm of quinidine sulfate was ordered every four hours. Ten hours after admission, the patient was much improved, sleeping well and exhibiting a much more regular cardiac rhythm. The extrasystoles, however, persisted. He complained of no pain. On the second hospital day the left calf was noted to be tender, and the right swollen. The temperature rose to 105°F. He complained of pain in the left chest on respiration, and bloody sputum was noted. The breath sounds were diminished over the left lower lobe. A bilateral femoral-vein ligation was done. After the operation he felt well, and the temperature returned to normal.

On the morning of the fifth hospital day the patient was in a cheerful mood, having spent a comfortable night. As the nurse was about to give him breakfast, he suddenly complained of pain in the back. He then began to breathe deeply, became flushed and died in a few seconds.

## DIFFERENTIAL DIAGNOSIS

DR EDWARD F BLAND The abruptness of the onset of illness in this previously well man and his sudden and unexpected demise a few days later, with pain, breathlessness and collapse, point unmistakably to a major vascular accident. The likeliest possibilities that immediately come to mind are pulmonary embolus, coronary thrombosis and dissecting aneurysm of the aorta. It is perhaps unnecessary to go beyond those three conditions in a discussion of the differential diagnosis. There are some clinical details, however, that are puzzling and warrant special comment.

Before we embark on the discussion, may we see the x-ray films? After Dr Hale has presented the

ries of films I have a few questions that I should like to ask him. I have not seen the films.

DR CLAYTON H. HALE: Unfortunately the films are all taken with the patient in bed and are not entirely satisfactory. We have here a heart that is somewhat enlarged, especially in the region of the ventricles. The aorta is tortuous, and there is suggestion in one of the films that the ascending aorta is slightly widened.

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pleuritic pain and the blood spitting strongly support this impression. This man's veins were tied. Could he have died of pulmonary embolus if both femoral veins were tied? It does not state in the text the site of ligation, whether it was above or below the femoris profunda. Dr Linton pointed out at Grand Rounds this morning that one group in this hospital prefers the lower site, whereas the other prefers the upper site. It is still possible that a large embolus could have come from the profunda if ligation was below this vein. Dr Linton also mentioned that even after ligation 5 per cent of patients may still have serious pulmonary emboli. I am inclined to think that this patient fits into the group in which an embolus either originated in the profunda or formed above the site of ligation. Does anyone know whether the profunda was below or above the site of ligation in this patient?

DR CASTLEMAN The superficial femoral veins were ligated just below the point where the profunda enters to form the common femoral.

DR BLAND It was possible, then, for an embolus to have come from above the site of the ligature or from the profunda.

We come next to a consideration of coronary thrombosis, and I am willing to exclude that diagnosis rather quickly. The onset was too abrupt. The patient had never had trouble previously. The electrocardiograms do not suggest coronary thrombosis, the patient was well between episodes, and he died abruptly. A few years ago Currens<sup>2</sup> pointed out the fact that, following pulmonary embolus, the accompanying shock and lowering of blood pressure predispose to coronary thrombosis or myocardial infarction. But as an added complication here that is unlikely.

The third condition is dissection of the aorta. The abrupt onset of pain during physical labor is always suggestive of such, especially when there is radiation of the pain through to the back bilaterally. It is not known whether or not the patient had had hypertension shortly before his illness. No mention is made of arterial pulsations in the legs, but I assume it would have been mentioned if they were absent, because the legs were the object of so much consideration.

DR PAUL D WHITE The pulsations were all right.

DR BLAND Is there anything else that points to aortic dissection? One thing that is disturbing is the diastolic murmur. We have to account for it on some basis, especially if we rely on the statement that it was not there one year before the patient came to the hospital. What could take place in the course of a year in a person who was otherwise in good health that would give a diastolic murmur of this nature? The description is not quite adequate to go into a discussion of whether it was a mitral or an aortic diastolic murmur or possibly came from some other valve. Since it

was so well heard over the base and since mitral diastolic murmurs, even loud ones, are not widely transmitted, I am inclined to think that this murmur came from the aortic valve. It is unlikely that rheumatic infection in a well man at this age could produce this much heart disease in the course of a year, at least a murmur of this degree and nature. It is unlikely that syphilis was responsible. The presence of a negative Kahn test one year before admission is strong evidence against it. What can arise acutely in the heart with a resulting diastolic murmur at the base? In patients with dissecting aneurysm of the aorta the dissection occasionally proceeds in a retrograde fashion, thereby distorting the orifice and resulting in a diastolic murmur. A ruptured aortic valve usually occurs acutely and often gives rise to a high degree of aortic regurgitation. We have no evidence of such here.

DR WHITE The chief murmur was diastolic in time, about Grade II and best heard along the left sternal border. It sounded like the murmur of aortic regurgitation. The systolic murmur was extremely slight.

DR BLAND Do you think that the diastolic murmur might have been overlooked a year before entry?

DR WHITE It was not heard at an outside hospital. We wondered if the examination had been careful enough to exclude it at that time. We did not believe that we could place much reliance on the recent development of the murmur, but nevertheless it was one of the findings seriously considered.

DR BLAND It is disturbing in relation to my favored diagnosis of pulmonary embolism. The weight of clinical evidence, however, favors phlebotrombosis, with multiple pulmonary emboli and a terminal massive embolus.

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it resemble coronary thrombosis in its onset it as too abrupt. We were also quite sure that with such a severe coronary occlusion there would have been a significant change in the electrocardiogram. I was disappointed after the x-ray diagnosis that the electrocardiogram did not show evidence of an acute cor pulmonale. If he had had a massive pulmonary embolism to produce this picture he ought to have had electrocardiographic evidence

## PATHOLOGICAL DISCUSSION

DR CASTLEMAN: The autopsy showed a dissecting aortic aneurysm. The intimal tear was in the ascending aorta—the usual place. The dissection had extended proximally and distally—proximally to the base of the aortic valve around the coronary mouths with some dissection of the coronaries themselves and distally to 4 cm above the bifurca-

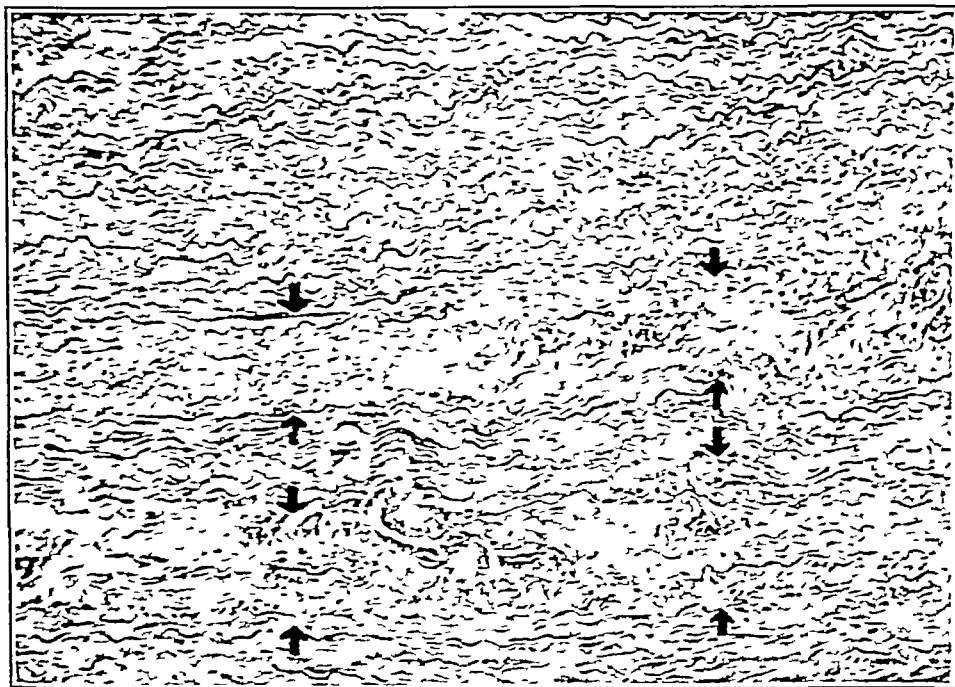


FIGURE 1 Pro-oncrograph Showing Medial Degeneration in the Wall of the Aorta. In the areas outlined by the arrows, there is total loss of the coarse black elastic fibers, this occurs before actual cyst formation takes place.

of an acute cor pulmonale, which he did not have. Yet as we went on, we wondered if he might not have been an exception to the rule.

DR BLAND: Which possibility did you favor, Dr. White?

DR WHITE: A dissecting aneurysm of the aorta because of the abrupt onset, the terrific pain and the essentially negative electrocardiogram.

## CLINICAL DIAGNOSIS

Dissecting aneurysm of aorta?  
Pulmonary embolism?

## DR BLAND'S DIAGNOSES

Phlebothrombosis femoral  
Pulmonary embolism and infarction

## ANATOMICAL DIAGNOSIS

Dissecting aneurysm of aorta with rupture into pericardium

tion of the aorta. It did not reach the iliac arteries, as is so often the case. There was some dissection into the branches at the arch. The aneurysm had ruptured through the adventitia at the level of the intimal tear into the pericardium with resultant cardiac tamponade.

DR WHITE: Were the renal arteries involved?

DR CASTLEMAN: No.

The lungs were quite disappointing. We were unable to find emboli or infarcts.

DR BLAND: But he was spitting blood and had pleuritic pain.

DR CASTLEMAN: There were areas of atelectasis and congestion but nothing that we could call a true infarct. It is quite possible, as you suggested, that they were incomplete infarcts that had begun to disappear. At any rate there was no massive embolus and no large infarct.

DR BLAND: Is that shadow part of the dissection of the aorta?

DR CASTLEMAN: The ascending aorta was diffusely dilated, which may have been the result of hypertension or perhaps a combination of hyper-

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## A NEW DEAL FOR THE VETERANS ADMINISTRATION

DURING the past several years many physicians who were not eligible for full military service have been urged to enter the Veterans Administration in a professional capacity. A few brave souls with excellent training in their respective fields accepted this challenge. Fully realizing that certain disadvantages surrounded their decision, they believed that there was a golden opportunity ahead of them. They recognized, on the one hand, that the medical care of veterans has heretofore been inexcusably poor and, on the other hand, that these very men who gave so much to their country deserve the best of medical and surgical care.

Some months ago there was talk of detailing medical officers of the Army and Navy to the Veterans Administration, and indeed several hundred were so transferred, the majority against their wishes. Had this movement been followed through, many of the difficulties of the past would have been eliminated, but as was pointed out in a recent editorial in the *Journal*,\* it would be far better for both the veteran and the physician to create a medical organization that in the fullest sense appealed to the returning medical officer and to the recent medical graduate. The veterans' hospitals should indeed be comparable with modern, first-class, teaching institutions.

A bill (H R 4717) introduced by the Democratic leader, Mr Rankin, and recently enacted into law by the signature of President Truman promises to do much to remedy existing conditions. It abolishes the medical service in the Veterans Administration as at present constituted and substitutes the Department of Medicine and Surgery which will establish a complete medical and hospital service, under the supervision of the Administrator of Veterans Affairs. There will be a medical director, a deputy medical director, eight assistant medical directors and a director of nursing. In addition, there would be a pharmacist, a dietitian, a physical therapist and an occupational therapist, as well as a dentist and an oral surgeon, each in charge of his particular division. The administrator, furthermore, has authority to establish residencies and to appoint qualified persons without regard to civil service or classification laws, rules or regulations, and there will be part-time consultants. For those in charge and all others employed, the specified salaries are fully adequate to attract a well trained personnel. In addition, a qualified specialist is entitled to 25 per cent additional pay, but no doctor shall be so rated unless he is a diplomate of his particular specialty board. Thus, it is apparent that the veterans should receive the best of medical and surgical care and that the positions available to physicians will be attractive, not only from the financial but also from the professional angle.

\*Editorial: Medical care for veterans. *New Eng J Med* 233:196, 1945

tension and medial degeneration, which was quite severe

DR WHITE I think that he had a hypertensive aorta. The x-ray films did not establish the diagnosis of dissection, but often the root of the aorta is as prominent in hypertension as in syphilis. I think that most of the right-sided vascular shadow is aorta rather than pulmonary artery.

DR CASTLEMAN We did not find much blood in the dissected part of the aorta.

DR WHITE Once in a while that is the case.

DR CASTLEMAN I believe that we have had only two cases with actual thrombosis in the dissecting channel. Usually the aneurysm is empty or has a few shreds of post-mortem clot. It is only when there is a large thrombus in the aneurysm that it might be possible to see an enlarged shadow by x-ray.

DR WHITE This could be simply the x-ray picture of a hypertensive aorta. A negative finding does not rule out a dissecting aneurysm, whereas a positive finding may be helpful.

DR CASTLEMAN This medial degeneration of the wall of the aorta was first described by Erdheim<sup>3,4</sup> and called by him "medionecrosis aortae idiopathica cystica," because occasionally the chromatropic degenerative material breaks down to form small cysts (Fig 1). This condition was described in this country for the first time by Dr Alan Moritz.<sup>5</sup> He is here today and perhaps will comment on it.

DR ALAN R. MORITZ I believe that there is still skepticism in some quarters regarding the occurrence of cystic medial necrosis of the aorta independent of atherosclerosis. I am sure that such skepticism is unjustified. It is true, however, that minor and, from a functional standpoint, inconsequential cystic

medial changes are frequently seen both with and without intimal disease and that such changes should be extensive if they are to be held responsible for aortic rupture. In my experience aortic rupture due to cystic medial necrosis is likely to run a more rapidly fatal course than that due to atherosclerosis.

DR WHITE In our series,<sup>6</sup> the reverse is true. Several days usually elapse before death.

DR MORITZ I have only seen ten or twelve cases of aortic rupture due to cystic medial necrosis, but I am sure that the majority of these patients died within minutes or, at the most, a few hours after the aorta gave way.

DR CASTLEMAN Our experience here is that in cases that have a dissecting aortic aneurysm the intimal tear has always been on the basis of medial necrosis, rather than being due to atheromatous ulceration. In fact, the intima is usually quite smooth in the region of the tear. In those cases in which dissection did originate from an arteriosclerotic ulceration, the dissection was very short and was an incidental autopsy finding, not having caused any clinical symptoms.

DR WHITE This man lived for four and a half days. Is that the average?

DR CASTLEMAN Yes.

#### REFERENCES

- 1 Hampton A O and Castleman B. Correlation of postmortem chest teleroentgenograms with autopsy findings with special reference to pulmonary embolism and infarction. *Am J Roentgenol* 43:305-326, 1940.
- 2 Currens J and Barnes A R. Heart in pulmonary embolism. *Arch Int Med* 71:325-344, 1943.
- 3 Erdheim J. Medionecrosis aortae idiopathica. *Virechows Arch. path Anat* 273:454-479, 1929.
- 4 Idem. Medionecrosis aortae idiopathica cystica. *Virechows Arch. path Anat* 276:187-229, 1930.
- 5 Moritz A R. Medionecrosis aortae idiopathica cystica. *Am J Path* 8:717-734, 1932.
- 6 Glendy R E, Castleman B, and White P D. Dissecting aneurysm of aorta: clinical and anatomical analysis of nineteen cases, thirteen acute with notes on differential diagnosis. *Am Heart J* 13:174-162, 1937.

tribed largely to greater awareness of the disease, which resulted in early diagnosis, better isolation and prompt treatment with antitoxin. After the rise of the Nazis, however, diphtheria began to increase in incidence and in severity, largely owing to the fact that immunization had not been practiced on any large scale.

During the period immediately preceding the outbreak of war, the countries neighboring on Germany were still having low diphtheria rates. So long as communications and the exchange of populations between Germany and her neighbors were still limited, the trends of diphtheria incidence remained the same in each of these countries. After the beginning of the war, however, Germany began to "export" diphtheria with her troops. The neighboring victims of German aggression were thus faced with a disease that had had a relatively low incidence for some time, during which a new generation of susceptibles had grown up because of the lack of effective programs of immunization. As a result, there was a tremendous increase in diphtheria in many of these countries at a time when it was almost impossible to apply effective countermeasures. The only country that did not share in this great increase of incidence was Hungary, in which an extensive immunization program had been practiced just prior to its occupation by Germany. This program paid dividends by holding the diphtheria rates to reasonably low levels, and the increase that did occur could be accounted for by changes in the population.

The number of cases of and deaths from diphtheria in the United States has shown a decline, with few remissions, since the beginning of this century, and there has been a steady and sharp drop since 1920. Immunization against this disease has been practiced only on a voluntary basis and in general has been quite spotty throughout the country. Without doubt, many American troops in Europe have become carriers of virulent diphtheria bacilli, irrespective of whether they have had the disease. Those who are yet to return will have had a greater exposure and will undoubtedly carry with them a greater volume of potential infection. To prevent any serious outbreak in this country it is

therefore urgent that efforts at extending immunization against diphtheria be redoubled.

An immune population is the best prevention against the occurrence of a diphtheria epidemic. The low incidence of diphtheria in this country in recent years has created a feeling of security that is totally unwarranted and that, in fact, may be the fuel on which an epidemic will feed unless the dampening effect of widespread immunization serves as an effective control. The facts that there has been a low incidence of the disease and that there are now a large number of susceptibles make the population particularly vulnerable, and an effective immunization program is essential.

## MASSACHUSETTS MEDICAL SOCIETY

### REVIEW LECTURE COURSE

The review lecture course for physicians in the Boston area that has been arranged by the Subcommittee on Postgraduate Medical Education of the Postwar Planning Committee, Massachusetts Medical Society, in co-operation with the Massachusetts Department of Public Health, will begin on February 18. The meetings will be held at Sanders Theater in Memorial Hall, Harvard University, Cambridge. These lectures, which are primarily designed for general practitioners and former medical officers, will review progress in medicine during the past four or five years. The speakers have been urged to present their subjects in a simple and direct manner and to emphasize diagnosis and treatment from the point of view of the physician in general practice.

All those who plan to attend but have not enrolled should do so immediately by either returning the post card recently forwarded to all physicians in Massachusetts or addressing a post card or letter directly to the Subcommittee on Postgraduate Medical Education, Massachusetts Medical Society, 8 Fenway, Boston 15.

The detailed program for the first four weeks of the course is as follows:

### REVIEW LECTURE COURSE

February 18 INFECTIOUS DISEASES *Chairmen* Charles A. Janeway and Edwin H. Place

5:00-5:45 Differential Diagnosis and Treatment of Infections of the Throat and Larynx Edwin H. Place, physician-in-chief, South Department, Boston City Hospital, clinical professor of pediatrics, Tufts College Medical School

There is, perhaps, one unfortunate provision, namely, that which states, "Any person to be eligible for appointment in the Department of Medicine and Surgery must — (a) Be a citizen of the United States — (b) In the medical service — hold a degree of doctor of medicine or of doctor of osteopathy." In some states, such as Massachusetts, a doctor, whether osteopathic or regular,

must pass the same examination before he may practice, in others, there is a separate licensing board for each. In the latter an osteopathic physician may be licensed to practice even though he could probably never pass the regular examination. The possible dangers of the situation are obvious, yet the act expressly states that "doctors must be graduates of a university approved

by the Administrator [and] have completed an internship satisfactory to the Administrator." Any possible danger is thereby lessened, if not eliminated.

There is no doubt but that this act offers to the veteran the best of service and to the doctor a great opportunity. With General Omar Bradley at the helm, one may be sure that his associates and subordinates will be of the highest personal and professional caliber, for his record has shown that, although cautious and careful in his judgment, once he moves, he brooks no interference. That Congress and the President have approved this legislation deserves commendation from civilian and veteran and physician alike.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

630,000 cases were notified in 1943 in those European countries that were still reporting infectious diseases fairly well. When countries are included from which reports were not available or incomplete, it may be safely assumed that there were about 1,000,000 cases throughout Europe in that year. This means that there were about 50,000 deaths from diphtheria, and these occurred mainly in the younger age

groups. The epidemic increased in proportions in most of the countries during the past two years, along with other infectious diseases, probably owing to the shifting of populations, poor nutrition, the breakdown of public-health programs and many other causes. There was a high prevalence of diphtheria among the German soldiers, and the liberating forces of the United Nations shared in this

increasing incidence of diphtheria throughout the European Theater of Operations. The usual forms of diphtheria of the upper respiratory tract, as well as severe wound infections, were encountered among the American forces in North Africa and later in Italy and on the rest of the Continent, and the disease is now prevalent among occupation troops. There has been a high incidence of cardiac and neurologic complications.

Last winter, Dr. Knud Stowman,\* chief of the Epidemiological Information Service of the United Nations Relief and Rehabilitation Administration, analyzed some of the salient epidemiologic features of the European outbreak. The results of his analysis may well serve as a stimulus to action aimed at the prevention of a similar resurgence of this disease in this hemisphere and particularly in this country.

As in most European countries, diphtheria morbidity and mortality in Germany showed a steady decline after the rise that accompanied the end of World War I. The downward trend has been as-

### "DIPHTHERIA REBOUNDS"

RECENT reports from Europe indicate that diphtheria has assumed epidemic prevalence and that the disease now encountered there is particularly virulent, with a high case fatality. About

\*Stowman K. Diphtheria rebounds. *Epidem Inform Bull* 1: 157 1945

## EXECUTIVE COMMITTEE OF THE COUNCIL

On January 9, 1946, the Executive Committee of the Council, on the recommendation of the Committee on Membership and representatives from the supervising censors, took the following actions

Allowed the following named fellows, applying for retirement and with all dues paid and in good standing, to retire under the provisions of Chapter I, Section 5, of the by-laws

Hunter, Norman M (Middlesex South), 98 Packard Street, Hudson

Overlander, J Elot (Hampden), 167 Maple Street, Springfield

Quest, James F (Suffolk), 409 Marlboro Street, Boston  
Victor, Agnes C (Worcester), P O Box 188, Worcester  
Williamson, Cordelia I (Suffolk), 464 Huntington Avenue, Boston

Allowed the following named fellows, applying for resignation and with all dues paid and in good standing, to resign under the provisions of Chapter I, Section 7, of the by-laws

Beaulieu, Florence A (Hampden), Monson State Hospital, Palmer

Margulios, Benjamin (Hampden), Monson State Hospital, Palmer

Allowed the following named fellow to change his membership from one district society to another, without change of legal residence, under the provisions of Chapter III, Section 3, of the by-laws

Moore, Francis D, 371 Walnut Street, Brookline (office Boston) (Norfolk to Suffolk)

Reinstated the following named physicians, under the provisions of Chapter I, Section 10, of the by-laws, who had been deprived of fellowship for the nonpayment of dues, provided their arrears in dues at the time of deprivation both to the Massachusetts Medical Society and to their district societies, plus their dues for the year 1946 both to the Massachusetts Medical Society and to their district societies be sent to the treasurer of the Society

Hagerty, Harry J (Worcester), 14 Ekman Street, Worcester

Sullivan, Leo J (Bristol South), 379 Whipple Street, Fall River

Remitted the dues owed the Society for the year 1946 of the following named fellow, who is ill and completely incapacitated and has been completely incapacitated for the past seven or eight years, under the provisions of Chapter I, Section 6, of the by-laws

Kaufman, M F (Worcester), 79 Elm Street, Worcester

The personnel of the Committee on Membership is as follows Harlan F Newton, *chairman*, Roy V Baketel, William A R Chapin, Peirce H Leavitt, and Samuel N Vose The representatives of the supervising censors were as follows William H

Allen, H Quimby Gallupe, and Albert E Parkhurst

MICHAEL A TIGHE, M D, *Secretary*  
Executive Committee

## DEATHS

KEITH — Theodore K Keith, M D, of Newton Center, died January 15 He was in his forty-fourth year

Dr Keith received his degree from Boston University School of Medicine in 1926 In 1943 he entered the Army Medical Corps, serving overseas for two years in England, France and Germany

His widow, two sons, his mother and father and a brother and sister survive

LEE — Frank R Lee, M D, of North Andover, died October 15 He was in his forty-third year

Dr Lee received his degree from Tufts College Medical School in 1927 He was a fellow of the American Medical Association

ROBBINS — Fred G Robbins, M D, of Salem, died May 16 He was in his seventy-sixth year

Dr Robbins received his degree from Harvard Medical School in 1892

His widow survives

## MISCELLANY

### MACY FOUNDATION DISCONTINUES REPRINT SERVICE

Doctor Willard C Rappleye, president of the Josiah Macy, Jr, Foundation, announces that more than five million copies of over four hundred leading medical and scientific articles have been published by the Foundation's War Reprint Service during the last three years for medical officers of the armed forces of the United States and, in so far as possible, of Canada, England, New Zealand, Australia, the Union of Socialist Soviet Republics and China Dr Rappleye stated that, with the plans for demobilization of the armed forces, the service was discontinued on January 1

The War Reprint Service has been an effort to bring new and important developments in the science and practice of medicine to medical officers who were largely cut off from sources of medical information during the war In the selection of these articles the Foundation has had the active co-operation of the Committee on Pathology of the Division of Medical Sciences, National Research Council, and of the National Committee for Mental Hygiene The articles selected for reprint and distribution were those dealing with the most recent scientific developments that had a direct bearing on medical and health problems related to military service The distribution to the medical officers was worked out in co-operation with the surgeons general of the Army and Navy and the Air Surgeon Through the courtesy of the National Committee for Mental Hygiene, more than one million reprints were delivered to medical officers specializing in neuropsychiatry

In addition to the articles reproduced from journals the Foundation published for the Air Surgeon five original monographs, prepared by medical officers of the Army Air Forces, dealing with personality disturbances occurring in combat zones Over ninety-five thousand copies of these monographs were distributed by the War Reprint Service as official documents of the Office of the Air Surgeon Eight additional monographs and nine reviews of medical literature on subjects of military interest were also prepared, and seventy thousand copies were distributed Since August, 1944, a *News Letter* for the Rheumatic Fever and Streptococcus Control Program of the Army Air Forces has been published monthly for the Air Surgeon, and over one thousand copies each month have been mailed to interested medical officers, military hospitals and medical-school libraries With the help of the Interdepartmental Committee on Cultural and Scientific Co-operation of the Department of State, sixty



5 45-6 30 Polomyelitis Conrad Wesselhoeft physician-in-chief, Haynes Memorial, Massachusetts Memorial Hospitals, clinical professor of communicable diseases, Harvard Medical School and Boston University School of Medicine

7 30-8 15 Colds, Influenza and Pneumonia Maxwell Finland chief, Fourth Medical Service, and associate physician, Thorndike Memorial Laboratory, Boston City Hospital, assistant professor of medicine, Harvard Medical School

8 15-9 00 Progress Report Charles A Janeway assistant professor of pediatrics, Harvard Medical School, visiting physician, Children's Hospital, associate in medicine Peter Bent Brigham Hospital

## February 20 CARDIOVASCULAR DISEASES *Chairmen* Herrman L Blumgart and Burton E Hamilton

3 00-3 45 Chronic Rheumatic Heart Disease Diagnosis and treatment Edward F Bland instructor in medicine, Harvard Medical School, visiting physician, House of the Good Samaritan, assistant visiting physician, Massachusetts General Hospital

3 45-4 30 Arterial Hypertension and Its Treatment Robert W Wilkins associate professor of medicine, Boston University School of Medicine, member, Evans Memorial, Massachusetts Memorial Hospitals

4 30-5 15 Electrocardiography in General Practice James M Faulkner professor of medicine, Tufts College Medical School

5 15-6 00 Treatment of Congestive Heart Failure Samuel A Levine assistant professor of medicine, Harvard Medical School, physician, Peter Bent Brigham Hospital

## February 25 CARDIOVASCULAR DISEASES *Chairmen* Herrman L Blumgart and Burton E Hamilton

5 00-5 45 Neurocirculatory Asthenia and Functional Cardiovascular Disturbances Paul D White lecturer in medicine, Harvard Medical School, physician, Massachusetts General Hospital

5 45-6 30 Cardiac Arrhythmias Their significance and treatment Louis Wolff instructor, Courses for Graduates, Harvard Medical School, chief, Cardiac Clinic, Beth Israel Hospital

7 30-9 00 Symposium on Coronary Artery Disease Pathology of Coronary Disease Monroe J Schlesinger pathologist, Beth Israel Hospital, visiting pathologist, Jewish Memorial Hospital

Diagnosis of Coronary Occlusion and Angina Pectoris Howard B Sprague associate physician, Massachusetts General Hospital, chief of Medical Staff, House of the Good Samaritan

Treatment of Coronary Occlusion and Angina Pectoris Joseph E F Riseman associate in medicine, Harvard Medical School, associate visiting physician, Beth Israel Hospital

## February 27 CARDIOVASCULAR DISEASES *Chairmen* Herrman L Blumgart and Burton E Hamilton

3 00-3 45 Congenital Heart Disease Indications for surgical treatment C Sidney Burwell physician, Peter Bent Brigham Hospital, consultant, Children's Hospital

3 45-4 30 Peripheral Vascular Disease and Its Treatment E Everett O'Neil clinical professor of surgery, Boston University School of Medicine, visiting surgeon, Boston City Hospital

4 30-5 15 Discussion of Cardiovascular Problems and Replies to Questions from Physicians Herrman L Blumgart physician-in-chief, Beth Israel Hospital, faculty instructor, Harvard Medical School

5 15-6 00 Discussion of Cardiovascular Problems and Replies to Questions from Physicians Burton E Hamilton cardiologist, Boston Lying-in Hospital, lecturer in Cardiology, Boston City Hospital

## March 4 PHARMACOLOGY AND THERAPEUTICS *Chairmen* Donald G Anderson and Chester S Keefer

5 00-5 45 Sedatives and Analgesics Robert W Wilkins assistant professor of medicine, Boston University School of Medicine, member, Evans Memorial, Massachusetts Memorial Hospitals

5 45-6 30 Streptomycin Chester S Keefer Wade Pro-

fessor of Medicine, Boston University School of Medicine, director, Evans Memorial, Massachusetts Memorial Hospitals

7 30-8 15 Penicillin Louis Weinstein assistant professor of medicine, Boston University School of Medicine, visiting physician, Haynes Memorial, Massachusetts Memorial Hospitals

8 15-8 45 Sulfonamides Francis C Lowell associate professor of medicine, Boston University School of Medicine, member, Evans Memorial, Massachusetts Memorial Hospitals

## March 6 NUTRITIONAL DISEASES AND VITAMIN THERAPY

*Chairmen* Harold J Jeghers and Fred J Stare

3 00-3 35 Nutritional Diseases in General Practice Harold J Jeghers assistant professor of medicine, Boston University School of Medicine, physician and chief of Fifth Medical Service, Boston City Hospital

3 35-4 10 A Review of Recent Advances in Nutrition Fred J Stare associate professor of nutrition, Harvard University, associate in medicine, Peter Bent Brigham Hospital

4 10-4 45 Nutritional Therapy Charles Davidson assistant in medicine, Harvard Medical School, resident physician, Thorndike Memorial Laboratory, and resident director, Second and Fourth Medical Services, Boston City Hospital

*PUBLIC HEALTH* *Chairman* Vlado A Getting

4 45-5 25 Recent Developments in Public Health Vlado A Getting Commissioner of Public Health, Commonwealth of Massachusetts

*INDUSTRIAL MEDICINE* *Chairman* Daniel L Lynch

5 25-6 00 The Objectives of Industrial Medicine George F Wilkins assistant medical director, New England Telephone and Telegraph Company, associate in surgery, Peter Bent Brigham Hospital

## March 11 BLOOD DISEASES *Chairmen* William B Castle and Joseph F Ross

5 00-5 50 The Use of Blood and Blood Derivatives Charles A Janeway assistant professor of pediatrics and instructor in bacteriology and immunology, Harvard Medical School, visiting physician, Children's Hospital, associate in medicine, Peter Bent Brigham Hospital

5 50-6 30 The Massachusetts Civilian Blood Program Geoffrey Edsall instructor in applied immunology, Harvard School of Public Health, assistant director, Division of Biologic Laboratories, Massachusetts Department of Public Health

7 30-8 15 Recent Advances in the Treatment of Blood Dyscrasias William B Castle professor of medicine and chairman of Department of Medicine, Harvard Medical School

8 15-9 00 The Rh Factor and Its Clinical Implications Louis K Diamond assistant professor of pediatrics, Harvard Medical School, visiting physician, Children's Hospital, director, Blood Grouping Laboratory, Boston

## March 13 X-RAY DIAGNOSIS AND THERAPY *Chairmen* Hugh F Hare and Merrill C Sosman

3 00-3 20 Progress in Diagnostic Roentgenology of the Lungs, Gastrointestinal Tract and Bones Laurence L Robbins roentgenologist, Massachusetts General Hospital

3 20-3 40 Progress in Diagnostic Roentgenology of the Genitourinary Tract, Gall Bladder, Heart and Skull George Levene professor of radiology, Boston University School of Medicine

3 40-4 00 Progress in the X-Ray Therapy of Malignant Lesions Frederick W O'Brien radiologist, Boston City Hospital

4 00-4 30 Progress in the X-Ray Therapy of Benign Conditions Hugh F Hare director, Department of Radiology, Lahey Clinic

4 30-5 00 Diagnosis of Peptic Ulcer Edward S Emery Jr, associate in medicine, Peter Bent Brigham Hospital

5 00-5 30 Treatment of Peptic Ulcer Franklin W White instructor in medicine, Harvard Medical School, consulting physician, Boston City Hospital

5 30-6 00 Gastroscopy and Gastritis Edward B Benedict associate visiting surgeon, Massachusetts General Hospital

# The New England Journal of Medicine

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Number 7

## THE REHABILITATION OF PATIENTS TOTALLY PARALYZED BELOW THE WAIST, WITH SPECIAL REFERENCE TO MAKING THEM AMBULATORY AND CAPABLE OF EARNING THEIR OWN LIVING\*

### II. Control of Urination

DONALD MUNRO, M.D.†

BOSTON

EVERY patient who has sustained an injury to the spinal cord, conus or cauda equina and is intelligent and co-operative has the right to expect infallible twenty-four-hour control of urination by the time he leaves his physician's care. Only those whose bladders have been denervated because of bilateral destruction of the parasympathetic plexuses or the lower four sacral segments or roots need any extraneous aid. Their numbers are negligible among civilians. Control of urination is an essential preliminary to self-support. No one will either walk abroad or be able to hold a job if he smells or if his clothes are wet with urine. There is no third choice between twenty-four-hour control with ambulation and self-support and a uriniferous aura with constant invalidism — usually in an institution — at the expense of the patient's family or the public.

It is the purpose of this paper to present evidence that therapy of the proper kind, properly applied with perseverance and patience over a sufficiently long time, will assure this end result to all such patients. No discussion of the details of the technique of treatment will be offered at this time. This will be considered by itself in a subsequent communication.

### MATERIAL

One hundred and twenty-five patients have been selected for this study from a group of 243 with injury to the spinal cord, conus or cauda equina. Every segment of the cord from the fourth cervical to the tip of the conus and all parts of the cauda equina are represented. One hundred and one of these 125 patients were chosen, first, because they had lived long enough — that is, one month or more — after the injury to permit some conclusions to be drawn as to the efficacy of the therapy, second, because a sufficient number of cystometrographic observations were made to verify the actual physiologic

state of response of the bladder at frequent intervals, third, because all had become stabilized at an end point in so far as the genitourinary system was concerned. In addition 24 patients in whom tidal drainage was either not needed or not used are included for comparison.

Thirty-one patients had an injury of the cervical cord, 49 of the dorsolumbar cord and 9 of the sacral cord and conus, whereas in 36 the cauda equina was damaged (Table 1). The patients with an anatomic transection had a total sensory and motor paralysis below the level of injury, with a complete severance of the cord and total separation of the cut ends. Those with a physiologic or functional transection had a total sensory and motor paralysis below the level of injury, but a small vestige of neural tissue bridged the gap and the transection, although physiologically complete, was not anatomically so.

### TREATMENT

Any treatment that leads to infallible twenty-four-hour control of micturition and meets the criteria listed at the opening of this paper must be considered satisfactory. I am not aware, however, of any procedure except tidal drainage that does this. Except where otherwise noted, this method was used as the fundamental therapy of the genitourinary tract in all cases reported herewith. Bladder stones, when present, were crushed intravesically. In the earlier cases, this was done without preliminary preparation. In the later ones, litholapaxy was postponed until after a period of bladder irrigation with Solution G<sup>1</sup>. Frequent intravenous and retrograde pyelograms were made as indicated. Originally a 1:30,000 solution of potassium permanganate was used as an irrigating fluid, but this was later changed to 0.5 per cent acetic acid, and in the last year or more this in turn has been discarded for either Solution M or Solution G<sup>1</sup>. Many other solutions have been tried but none of them compare in efficacy with acetic acid and the buffered

\*From the Department of Neurosurgery, Boston City Hospital.  
†Assistant professor of neurosurgery, Harvard Medical School; associate professor of neurosurgery, Boston University School of Medicine; chief, Department of Neurosurgery, Boston City Hospital.

thousand reprints were distributed to medical teachers and investigators in forty-eight foreign countries. The Office of War Information requested permission to circulate the Foundation's reprints among more than thirty of their foreign outposts and reduplicated selected articles for their distribution to medical leaders abroad.

## NOTICES

### ANNOUNCEMENTS

Dr R Earle Glendy, having returned from service with the United States Army, announces the opening of his office at 820 South Jefferson Street, Roanoke, Virginia, for the practice of internal medicine, with special interest in diseases of the heart and circulation.

Dr Langdon Parsons, having returned from military service, is resuming the practice of surgery at 264 Beacon Street, Boston.

### BOSTON MEDICAL HISTORY CLUB

There will be a meeting of the Boston Medical History Club in Sprague Hall at the Boston Medical Library, 8 Fenway, on Monday, February 11, at 8 15 p m. Dr Charles F Branch will speak on the subject "Some Aspects of the History of Cancer."

All interested persons are cordially invited to attend this meeting.

### NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Hotel Kenmore, Boston, on Wednesday, February 20, at 8 p m. Dr David C Ditmore will speak on the subject "The Diagnosis and Treatment of Hemorrhoids, with Special Reference to Physical Medicine."

### NEW ENGLAND HEART ASSOCIATION

The annual Henry Jackson Lecture under the auspices of the New England Heart Association will be given by Dr Tracy B Mallory at 8 15 p m on Tuesday, February 26, at the Boston Medical Library. His subject will be "Certain Features of the Pathology of Traumatic Shock."

Interested physicians and medical students are cordially invited to attend.

### NEW ENGLAND PEDIATRIC SOCIETY

The annual meeting of the New England Pediatric Society will be held in Boston on Thursday, February 28.

### HERMANN M BIGGS MEMORIAL LECTURE

The Hermann M Biggs Memorial Lecture under the auspices of the Committee on Public Health Relations, New York Academy of Medicine, will be delivered by Dr Laurence H Snyder, professor of medical genetics, Ohio State University, at 8 30 p m on Thursday, April 4, in Hosack Hall, New York Academy of Medicine. His subject will be "Medical Genetics and Public Health."

All persons interested are invited to attend.

### ELLA SACHS PLOTZ FOUNDATION FOR THE ADVANCEMENT OF SCIENTIFIC INVESTIGATION

During the twenty-second year of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation, thirty-eight applications for grants were received by the Trustees, twenty-five of which came from the United States, the other thirteen coming from five different countries in Europe, Asia, North and South America. Twenty-two grants were distributed.

Applications for grants to be held during the year 1946-1947 must be in the hands of the Executive Committee before April 15, 1946. There are no formal application blanks but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. In their requests for aid applicants should state whether or not they have approached other foundations for financial assistance and what other sources of support are relied on for research. It is highly desirable to include letters of recommendation from the directors of the departments in which the work is to be done. Only applications complying with the above conditions will be considered. Applications should be sent to Dr Joseph C Aub, Massachusetts General Hospital, Fruit Street, Boston 14.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 14

#### FRIDAY, FEBRUARY 15

\*9 00-10 00 a m Diagnosis of Congenital Heart Disease by Venous Catheterization. Dr Lewis Dexter. Joseph H Pratt Diagnostic Hospital.

\*10 00 a m-12 00 m Medical Staff Rounds. Peter Bent Brigham Hospital.

10 50 a m Topical Therapy in Dermatology. Dr Bernard Appel. (Postgraduate Clinic in Dermatology and Syphilology) Amphitheater, Dowling Building. Boston City Hospital.

#### MONDAY, FEBRUARY 18

\*12 00 m-1 00 p m Clinicopathological Conference. Peter Bent Brigham Hospital.

#### TUESDAY, FEBRUARY 19

\*12 15-1 15 p m Clinicorontgenological Conference. Peter Bent Brigham Hospital.

#### WEDNESDAY, FEBRUARY 20

\*9 00-10 00 a m Psychologic Aspects of the Menstrual Cycle. Dr Norris T Flanagan. Joseph H Pratt Diagnostic Hospital.

\*10 30-11 30 a m Medical Clinic. Isolation Building Amphitheater. Children's Hospital.

\*12 00 m Clinicopathological Conference (Children's Hospital) Amphitheater. Peter Bent Brigham Hospital.

\*2 30-4 00 p m Combined Clinic by the Medical Surgical and Orthopedic Services. Amphitheater. Children's Hospital.

\*Open to the medical profession.

JANUARY 7-APRIL 22 1946 Metropolitan State Hospital. Eleventh Postgraduate Seminar in Neurology and Psychiatry. Page 314 issue of September 6.

FEBRUARY 4-MARCH 29 Health Education Institute. Page 746, issue of December 13.

FEBRUARY 9 New England Dermatological Society. Page xix, issue of January 17.

FEBRUARY 11 Boston Medical History Club. Notice above.

FEBRUARY 12 Harvard Medical Society. Peter Bent Brigham Hospital. 8 00 p m.

FEBRUARY 13 Massachusetts Medico-Legal Society. Page xix, issue of January 17.

FEBRUARY 14 Diagnostic and Therapeutic Suggestions in Cardiovascular Disease. Dr John Sproull. Pentucket Association of Physicians. 8 30 p m. Haverhill.

FEBRUARY 19 Greater Boston Medical Society. Page 168, issue of January 31.

FEBRUARY 20 Tufts Medical Alumni Lecture. Page xix, issue of January 17.

FEBRUARY 20 New England Society of Physical Medicine. Notice above.

FEBRUARY 26 New England Heart Association. Notice above.

FEBRUARY 27 Tufts Alpha Omega Alpha. Page 168, issue of January 31.

FEBRUARY 28 New England Pediatric Society. Notice above.

APRIL 4 Hermann M Biggs Memorial Lecture. Notice above.

MAY 13-17 American College of Physicians. Page 798 issue of December 20.

### DISTRICT MEDICAL SOCIETY

#### WORCESTER

FEBRUARY 13 Worcester State Hospital.

MARCH 13 Worcester Memorial Hospital.

APRIL 10 Hahnemann Hospital.

MAY 8 Annual meeting.

reflex level, depending on the type of cord injury, cystometrograms should be done at least once a week, and oftener if indicated. Only in this way can the physician so adjust his therapy as to suit it to the needs of the particular bladder under treat-

cystometrograms and further simplifies collecting the required observations.

Tidal drainage as a therapeutic procedure has also been criticized as needing a specially trained technician to operate it efficiently, as requiring such constant attention as to necessitate extra ward personnel—especially at night—and as causing necrosis of the bladder.<sup>9</sup> It is a matter of record that the system has been effectively used in China (Fig 3), in various clinics in the United States,<sup>10-14</sup> England,<sup>6, 15-18</sup> Canada,<sup>7, 19</sup> and Mexico,<sup>20</sup> in American Army hospitals in this country<sup>21-25</sup> and in England<sup>26</sup> and on islands in the South Pacific. It has also been used on airplanes and on vessels during transatlantic crossings.<sup>27</sup> Lowsley and Kirwin,<sup>12</sup> Swartz,<sup>19</sup> McLellan,<sup>10</sup> Cone and Bridgers,<sup>7</sup>

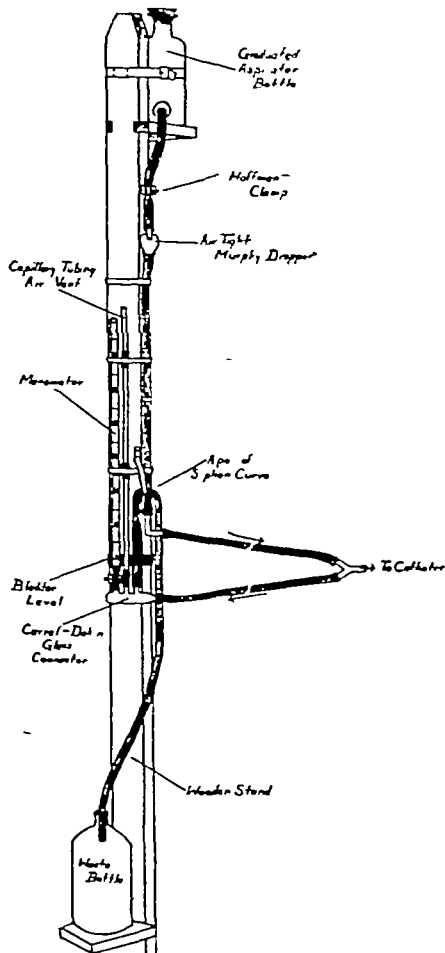


FIGURE 1 The Tidal-Drainage Apparatus as Modified by McNeil and Bowler<sup>5</sup> and O. H. Stewart<sup>6</sup> (with built-in cystometer)

ment, and only thus can tidal drainage or any other equally effective method of treatment operate efficiently and act as a therapeutic agent.

Criticism of the use of tidal drainage in cord-injury cases has been made because of this need. It has been said that it is not worth while and that it takes too much time to go to all this trouble to make so many observations. In the final analysis, this is a matter of the amount of interest the physician has in taking the necessary steps to see that his patient gets the best possible functional end result. Failure to employ all possible means for this purpose is a criticism not of any therapeutic procedure but of the physician performing it. The modern tidal-drainage apparatus (Figs 1 and 2),<sup>7, 8</sup> which has a built-in cystometer, obviates the need for setting up a special apparatus for making the

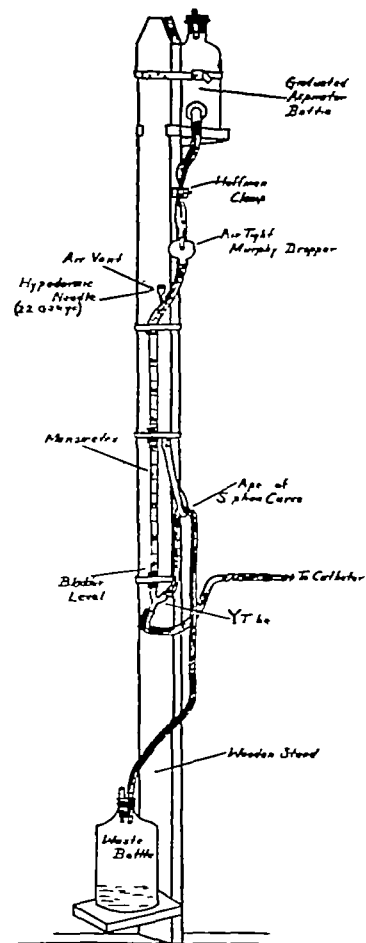


FIGURE 2 The Tidal-Drainage Apparatus as Modified by Cone and Bridgers<sup>7</sup> (with built-in cystometer)

McCrea,<sup>13</sup> Thomas<sup>14</sup> and the United States Army,<sup>21, 24-26</sup> in this country and Canada, as well as Robinson,<sup>16</sup> Stewart,<sup>6</sup> Kerr,<sup>17</sup> Wells<sup>15</sup> and others in England and elsewhere, have written describing its successful use. In this clinic, medical students, interns within a year of graduation from

citric acid solutions, and of these the latter are far and away the better. The only complication that has followed their use has been an occasional scrotal dermatitis when too much leakage around the catheter or lack of cleanliness has been permitted. In the male, a No 16 or 18 Fr soft-rubber rectal tube, held in place with adhesive-tape strapping around the penis, and in the female, either a similar rectal tube taped to the pubis or a perforated mushroom-tipped soft-rubber catheter of the same size have been used almost without exception as catheters. A Foley-type catheter has been used only rarely and has never been considered essential. The catheters have been removed, cleaned and resterilized, and replaced or a new one has been substituted once a week, at which time a urine culture<sup>2</sup> has been made. For the last six years no drugs

present was cured or brought under control before attempting to start the training period. Culturable bacteriuria has been constantly present so long as the catheter was in use,<sup>2</sup> but it has disappeared in almost every patient and regardless of the kind of infecting bacteria following removal of the catheter and without the use of medication when either normal micturition has been established or the training period has been completed. Any operation, exhaustion, impairment of nutrition, anemia, concurrent infectious disease or surgical infection anywhere in the body causes the bladder function to regress, even to the point of becoming atonic if normal micturition has not already been re-established. Conversely, good general health and nutrition and in particular a normal blood content and circulation, together with physical activity and

TABLE 1 *Diagnoses*

LEVEL OF INJURY	NO OF CASES	TRANSECTING LESIONS		NONTRANSECTING LESIONS										TOTAL DRAINAGE NOT USED OR NOT NEEDED
		ANATOMIC	FUNCTIONAL	HEMORRHOIDS	HEMATOXYLIA	CONPRESSION	CONTUSION	EDEMA	SUBARACHNOID HEMORRHAGE	ADHESIVE ARACHNOIDITIS	RADICULITIS	BULLET WOUND	BRUIA MITIDA	
Cervical	31	0	2		21	3	4	1	0	0	0	0	0	1
Dorsolumbar	49	24	14	0	3	6	0	2	0	0	0	0	0	6
Sacral, including conus	9	0	0		0	0	1	0	0	2	0	0	0	1
Cauda equinal	36	0	0	4	0	16	4	0	0	1	6	2	2	16
Totals	125	24	16	4	24	30	9	3	1	3	6	2	2	24

have been employed to sterilize the urine. In the earlier cases many different ones were tried by mouth, intravenously and in solution for use in the bladder, but none of them produced any effect. The fluid intake is kept at 4500 cc every twenty-four hours for adults with a normal circulation. This amount is scaled down to an appropriate level for children and cardiac invalids. As soon as the activity of the bladder becomes established at a reflex level, a period of training in bladder control is begun. In patients with a transection, this produces sufficient bladder capacity so that they can go a minimum of three hours during the day and while active, and the entire night without wetting themselves or being awakened. The bladder nevertheless continues to function on the "reflex" as opposed to the "normal" level.<sup>3</sup> In nontransecting injuries a normal bladder results. Except in cases with a destructive lesion of the sacral cord, with a resultant denervation of the bladder, all patients, regardless of the original injury, have had either a normal or a reflex bladder at discharge and have been free of catheters and any form of urinal, as well as of the need for using tidal drainage. Contracted or shrunken bladders have been stretched to a capacity of 200 cc before reflex emptying. Any cystitis or pyelitis that was

exercise within the limits of the patient's capacity, facilitate progress toward normalcy and controlled reflex micturition. Experience has demonstrated that aside from intelligent co-operation on the part of the patient during the training period, the two most important factors in attaining a satisfactory end result are a knowledge at all times of the functional stage that the bladder has reached in its progress toward either complete recovery or a reflex level and the need for instituting therapy by tidal drainage at the earliest possible moment and preferably at once after receipt of the injury. The first is possible only if frequent cystometrograms<sup>4</sup> are made. The initial one should be made when the patient is first seen or as soon thereafter as possible. It is no more reasonable to expect to treat a case of surgical shock or circulatory collapse, for example, without a blood-pressure reading at the first visit than it is to treat the bladder of a patient with a spinal cord injury without a cystometrogram at the earliest possible moment. The function of the bladder can not be estimated without a cystometer any better than the state of the circulation can be judged without a sphygmomanometer. This analogy is equally true in the later stages. Until the bladder function has been stabilized at either the normal or the

## COMPLICATIONS

The complications relative to the bladder the urethra and the paraurethral structures that developed in this series have been analyzed in relation to their presence at the time of admission in patients in whom tidal drainage was either not begun for an appreciable interval after the receipt of the injury, was not needed or was not used when it should have been and in relation to their recur-

vaginal fistula. A vasectomy was performed on 1 patient. Thus, 26 per cent had complications already present before tidal drainage was started. By comparison, of the 52 patients treated with tidal drainage from the receipt of the injury, 3 had bladder stones, 4 urethritis, 1 a periurethral abscess, 1 prostatitis, and 2 epididymitis. One patient had a vasectomy. Thus, 23 per cent had complications traceable to the therapy. It is worth noting, however, that in 26 patients, 11 of whom had transec-

TABLE 2 Urethral and Perurethral Complications

COMPLICATION	NO OF CASES	CAUSE OF URETHRAL AND PERIURETHRAL SEPSIS			END RESULTS				
		LARGE CATHETER	STYLETTED CATHETER	UNKNOWN PRESENT ON ADMISSION	DIED (CAUSE)				STILL ON RECOVERED WARD
					Sepsis of Genito-urinary Tract	Infected Operative Wound	Sepsis from Bedsores	Miscellaneous	
Urethritis	4	4	0	0	0	0	0	1	0
Epididymitis	5	4	0	1	0	0	1	0	0
Prostatitis	1	1	0	0	0	0	0	0	0
Periurethral abscess (Vasectomy†)	5*	0	2	3*	2	1	0	0	1
	(2)	(2)			(1)				(1)
Totals	14	9	2	3	2	1	1	1	1
No urethral or periurethral complications	67				2	2	3	11	4
Grand totals	101				4	3	4	12	5

\*One case previously listed under "epididymitis"

†Not counted as a complication

rence during treatment by this method. It has proved impossible to determine accurately the presence or absence of pyelitis and its relation to the use of this therapy, and this complication is therefore not included. It can be definitely stated, however, that all the patients who had pyelitis during their hospital stay were free of it at the time of discharge. One patient in whom tidal drainage was begun after an interval and one who was not

tions, who have come under treatment in the last six years the only complications have been bladder stones in the 3 cases just mentioned and urethritis and prostatitis in 1 case each. It has only been since the commencement of this period that the apparatus and the technic of managing it have reached a high level of efficiency. The percentage of complications in this group was 19. It is probable that this incidence can be lowered still further now

TABLE 3 Infection of the Genitourinary Tract

TIME OF TIDAL DRAINAGE	NO OF CASES	PRESENT AT ADMISSION				DEVELOPED UNDER TREATMENT				PRESENT AT DISCHARGE (ALL CASES)		NONE AT ANY TIME		STILL UNDER TREATMENT	
		NO	PER-CENTAGE	PRESENT AT DISCHARGE	PER-CENTAGE	NO	PER-CENTAGE	PRESENT AT DISCHARGE	PER-CENTAGE	NO	PER-CENTAGE	NO	PER-CENTAGE	NO	PER-CENTAGE
From the start	52	4	8	3	75	12	24	1	8	4	8	6	69	0	0
After an interval	49	48	98	8	16	1	2	1	100	9	20	0	0	5	10
Not used	24	5	21	4	80	0	0	0	0	4	17	19	79	0	0
Totals	125	57		15		13		2		17		55		5	
Averages			46		26		10		15		14		44		4

treated at any time by this method each had a stone in one kidney. The stones were removed by appropriate surgery. Of the 65 patients in whom complications were present before tidal drainage was used or in whom it was decided not to employ it 6 had bladder stones, 4 a periurethral abscess, 3 epididymitis, 1 a dilated urethra, and 1 a vesico-

that the development of bladder stones appears to be reduced to a minimum by the use of the buffered citric acid solutions (Solutions M and G).

## OTHER METHODS OF TREATMENT

A number of other methods of treating the bladder in patients with injury to the spinal cord, conus

medical school and nurses have all learned to set it up and supervise the operation with a week or ten days' training and with no more supervision than is required for any other ordinary procedure in a surgical ward. No personnel beyond the single nurse on duty at night or the usual ward staff at any other time has ever been required to care for anywhere from three to twelve patients being treated simultaneously in this way. Any trouble

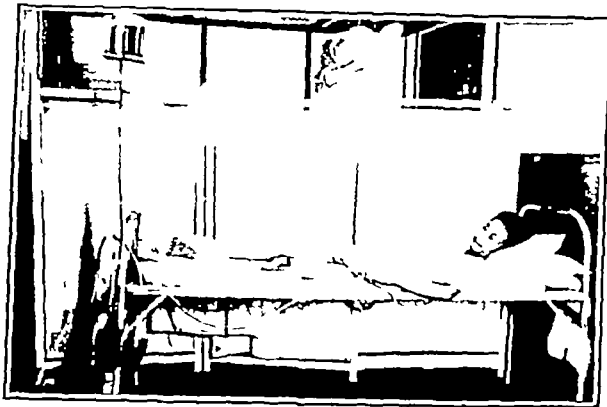
autopsy when tidal drainage has been previously used nor at cystoscopy, nor has it been suggested by any clinical symptoms in the surviving patients. In the face of such experience and in the absence of details in support of their claim, this statement made by Barrington, Everidge and Morson must be disregarded, and any other conclusions drawn by them on this subject must be looked at with suspicion.

Objection has also been raised to the use of tidal drainage because an inlying catheter is necessary. It is claimed<sup>9, 18, 23, 25, 28</sup> that the presence of a catheter in the urethra for any appreciable time causes urethritis, epididymitis, periurethral abscesses, necrosis of the mucous membrane, strictures and so forth. It is generally agreed that the urethra is constantly contaminated and that the complications listed above are primarily the results of pressure necrosis from the catheter, with subsequent infection of the dead tissue. Interference with the drainage of the normal urethral secretions is a contributory cause. Despite this fact, a large catheter that completely fills the urethra is frequently used in males with the object of controlling leakage from the bladder. I am convinced that urethral complications only follow the use of a catheter that is *too large* or that has been inserted with the aid of a stylette (Table 2). Leakage of urine around the catheter depends not on the size of the tubing but rather on the integrity of the sphincters that surround and compress it. When closed, such sphincters assure retention of the urine in the bladder no matter what the size of the catheter that passes through them, but when they are open, leakage is inevitable despite all attempts to plug the bladder. I am certain that it is neither necessary nor good practice to use an inlying catheter larger than No. 16 or 18 Fr. If this rule is adhered to and the catheter is removed, cleaned, resterilized and reinserted in a sterile manner once a week, no urethral or periurethral complications such as those listed above will develop.

The importance of beginning tidal-drainage treatment early if complications are to be avoided and a satisfactory end result reached is apparent from Table 3. In particular, it should be noted that whereas the genitourinary tract was infected in 98 per cent of the cases at the beginning of tidal drainage, when use of the latter was delayed until some time after the receipt of the accident, only 8 per cent were similarly infected when it was used from the first. Although 12 patients (24 per cent) developed infection of the genitourinary tract while being treated with tidal drainage, infection was present in only 8 per cent of this group at discharge, in contrast to 20 per cent in the other group and 17 per cent in the patients that had no such therapy at any time. Sixty-nine per cent of the first group had no infection at any time. That this therapy was efficient is evidenced by these figures.

## 脊髓膀胱 (Cord bladder) 之治療

李 宗 華 葉 復 霖



脊髓膀胱之初期人抵抗弱而早過後膨脹之現象如醫治不得其法則膀胱漸形緊縮自一九三四年孟氏 (Munro) 將連續灌流法 (Tidal drainage) 應用於脊髓膀胱醫治之後上述症狀概可預防不特膀胱之發炎可以減少而石炭病人亦較便利膀胱膨脹亦不易發生據孟氏個人四年之經驗該項病症之死亡率可減至百分之十強足證連續灌流法之於脊髓膀胱之治療有顯著之功效連續灌流法之應用須先對於各型之脊髓膀胱有明瞭之認識

501

FIGURE 3

that has arisen has been traceable at all times to improper adjustment of the apparatus to the bladder that it was serving.

The criticism that this apparatus causes gangrene of the bladder, made by Barrington, Everidge and Morson,<sup>9</sup> merits more serious attention. This occurred in the course of a joint meeting of the sections of Urology and Neurology of the Royal Society of Medicine. Nothing beyond the bold statement appears to substantiate this claim. No one else, so far as I am aware, has made a similar statement, and none of the other speakers on the same program are reported to have made such a criticism. These authors made no mention of the number or type of cases that developed gangrene and were treated with tidal drainage or in any other way. No suspicion of such a complication has ever arisen in any of my 101 patients nor in any others who were similarly treated in this clinic for less than a month. The condition has never been found at

not use absorptive pads around the tube and is not constantly faced with the choice of disposing of damp or wet pads or smelling of stale urine. There is the further consideration that an inlying suprapubic tube causes pain when the body is in certain positions and thus limits physical activity, is prone to rot and break in two leaving a free foreign body in the bladder, serves as a source of irritation, infection and stone formation fails to prevent puddling, with consequent infection of the genitourinary tract, anchors the bladder abnormally

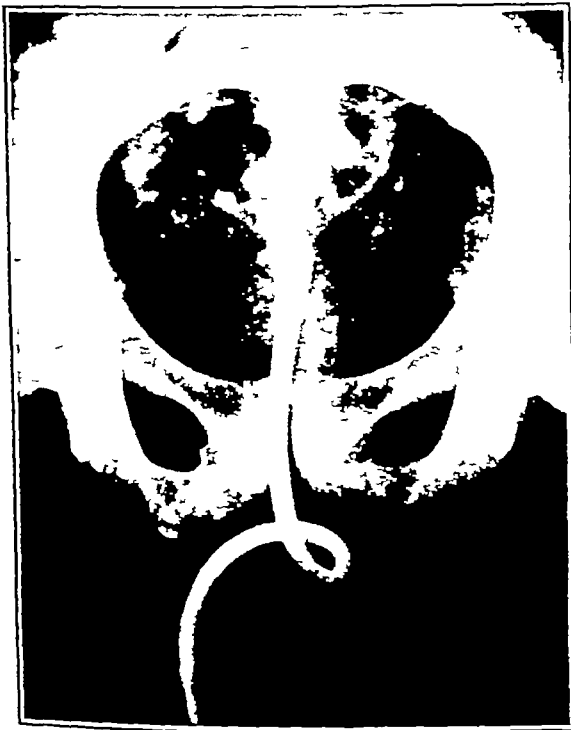


FIGURE 4 Roentgenogram of a Dilated Urethra, with Looping and Kinking of the Catheter in the Dilated Portion. This patient had an anatomic transection of the thoracic cord and had been using a penile clamp for one month.

to the abdominal wall, and promotes shrinkage and fibrosis of the bladder wall with a progressive decrease in capacity and consequent increasing uselessness of the organ as a reservoir.

The only justification for this operation as a means of treating the bladders of patients with injury to the spinal cord or cauda equina lies in the circumstances that surround combat conditions in war and the difficulties of transport that go with them. It may well be impossible to provide sufficient supervision to maintain proper catheter drainage under such conditions. Because this is essential, the lesser risk of draining the bladder suprapubically rather than by the preferable route through the urethra must be taken to avoid the greater risk of no drainage

at all. There is no reason why it should be necessary to employ it, however, except in these or analogous circumstances. If it has been used, steps should be taken to close the fistula at the earliest possible moment. This should not be undertaken, however, until after cystoscopic examination with intravenous and if necessary retrograde pyelography and a study of specimens of urine from the kidney pelvis have eliminated the presence of stones anywhere in the genitourinary tract, major pyelitis or pyelonephritis, encrusting or ulcerative cystitis and an occluded urethra. If such conditions exist, appropriate operative treatment of the kidney and intermittent manual irrigation of the bladder with Solution G should be carried out, and restoration of the urethral patency should be established before closing the fistula.

Such irrigation has been most effective in my hands when the fluid enters the bladder by way of an inlying urethral catheter, with the suprapubic tube kept closed until leakage takes place around the latter. In this way a maximum amount of the irrigating solution is introduced into the bladder, and at the same time the bladder wall is gently stretched and its capacity is gradually increased. Between irrigations the bladder should be allowed to drain through the catheter and not through the suprapubic opening. After these preliminaries have been completed, the suprapubic fistula can be closed.

It is undoubtedly true that almost all such fistulas eventually close spontaneously after removal of the suprapubic tube and without further local therapy, and it is customary to allow them to do so. This seems to be an extremely unsurgical method of dealing with this problem. The trouble that is saved by permitting closure in this way rather than by resorting to surgical closure with excision of the fistulous tract and surrounding scar does not justify the restriction of bladder activity that must be associated with the former method and that is reduced to a minimum by the latter one. So long as the fistulous tract is present the bladder will be anchored to the abdominal wall, which is neither anatomically nor physiologically correct.

In the group of patients under discussion, the bladder, even under the best of circumstances, works under a tremendous handicap. The more nearly perfect its anatomic and physiologic relations to the surrounding tissues, the nearer is its approach to normal function. A surgical closure and excision of the fistula and scar, with layer sutures of the bladder and overlying tissues and appropriate post-operative drainage of the space of Retzius, leaves a minimal amount of perivesical scarring and adhesion and permits maximal mobility of the bladder in the course of filling and consequent maximal storage capacity. Overstretching of the wound and leakage through the surgical incision can be prevented by constant urethral drainage during wound



or cauda equina have been advocated. I have been unable to find that any advocate of these alternative methods has claimed infallible twenty-four-hour control of urination as the result of their use. Even in clinics in which tidal drainage has been used,<sup>6, 7, 10, 11, 15, 17, 19, 21, 22, 26</sup> I am not aware of any published results in, for example, patients with transected cords that offer any better genitourinary end result than a so-called "automatic bladder." Such a bladder is in fact, and as evidenced by cystometric studies, a reflex bladder.<sup>3</sup> Instead of the patient's being given infallible twenty-four-hour control of micturition without the aid of apparatus, dryness and safety are secured only with the help of urinals and pads, and a night's sleep only at the cost of dangerous reduction of the fluid intake with consequent risk of pyelitis, or, when accompanied by a wet bed, frequent waking, the discomfort of rubber sheets, inability to spend a night away from home and the like.

The perennial argument whether it is better, particularly in the early stages, to permit the bladders of patients with injury to the cord or cauda equina to overflow or to empty them periodically by intermittent catheterization or by manual expression of their contents stems from ignorance of the processes by which a bladder that has been so paralyzed recovers. Automaticity is the best that can be expected from such treatment, and this can be gained only at the risk of permanent damage to the bladder wall and major infection of the genitourinary tract. This subject has been well covered elsewhere,<sup>3, 16, 29, 30</sup> and the discussion need not be repeated here. Proper cystometric investigation will demonstrate that none of these three methods are appropriate and that all are dangerous. If the patient is so fortunate as to acquire an "automatic bladder" this same lack of knowledge deprives him of an ideal end result, only because his physician fails to afford him the opportunity for the final training that makes the difference between a complete functional success and a makeshift near-failure.

#### *Intermittent Irrigation*

Manually controlled intermittent irrigation used alone leads at best only to an "automatic" or reflex bladder. This method has been described by Lowsley and Kirwin<sup>12</sup> and advised, among others, by the Medical Department of the United States Army.<sup>24</sup> There is no question that this method when properly used by an intelligent patient and under the direction of a careful and competent physician is the best substitute for tidal drainage. It will, without doubt, permit the development of a reflex bladder without infection of the genitourinary tract in an unknown percentage of patients with injury to the cord or cauda equina. It cannot be denied, however, that it is inaccurate, time-consuming, unphysiologic and relatively ineffective

unless checked by frequent cystometric observations. A period of bladder training must follow its employment if practical useful urinary control is to be expected. I have personal knowledge of two clinics in which this method was used. In one it was a brilliant success, and in the other it was a dismal failure. The difference in results was directly traceable to the efficiency of the physicians in charge. The automatic feature of tidal drainage does away with this hazard. Next to tidal drainage, however, manually controlled intermittent irrigation appears to be the most satisfactory therapy for the cord bladder, and if properly handled and followed by bladder training it can be used instead of it.

#### *Penile Clamp*

The simplest method of urinary control in males is that associated with the use of a penile clamp. Urinary leakage can unquestionably be prevented by this means, but only at the expense of a possible dilated urethra in cases of cord injury. Whenever a reflex bladder has been established, an emptying contraction of the detrusor muscle, with associated relaxation of the internal and external sphincters, develops in response to a critical amount of stretch of the bladder wall. If a mass reflex is present, the bladder may also empty at any time and regardless of the amount of fill.<sup>31</sup> Once such a contraction starts, it continues until either the bladder is emptied or the detrusor is exhausted and again relaxed because of its inability to overcome an external resistance that is greater than the force of its contraction. It is this latter condition that accompanies the use of a penile clamp. The forceful expulsion of the urine from the bladder into the urethra up to the point of compression by the clamp dilates the urethra (Fig. 4) and bladder and causes puddling of the bladder urine, with cystitis and attacks of pyelitis as inevitable consequences. This can only be avoided by release of the clamp whenever such an emptying contraction occurs. Such a regimen predicates a knowledge of bladder training as referred to above and the abolition of the mass reflex when necessary.<sup>31</sup> Under such circumstances, a penile clamp is superfluous. Its employment is justified, therefore, only in exceptional circumstances, and then merely as insurance against failure on the part of the patient to urinate at regular intervals and in the absence of a mass reflex.

#### *Suprapubic Cystostomy*

Suprapubic cystostomy both as a temporary and as a permanent method of treating cord bladders has many advocates. Its use as a permanent method in cases of cord injury cases appears to be illogical and indefensible. Surgeons claim that when the cystostomy is properly performed the bladder does not leak. I have yet to see a patient with a cord injury whose bladder has been drained in this way who will agree with this statement or who does

uch factors as associated sepsis, hypoproteinemia, arly death, mental changes, lack of co-operation and concomitant disease, all conditions that had no direct connection with the therapy. Only 5 cases of failure (5 per cent) are attributable to the use of tidal drainage. Four of these were in early patients who were cared for while the apparatus was still being developed, they can also be eliminated from consideration. It may be concluded, then, that only 1 of 101 patients (0.9 per cent) with an injury to the spinal cord or cauda equina who

the spinal cord, conus or cauda equina and is intelligent and co-operative can have infallible twenty-four-hour control of urination by the time he leaves his doctor's care.

If tidal drainage is used at once after receipt of the injury and supplemented by frequent cystometrograms, the chance of obtaining this result is 20 per cent greater than if its use is delayed.

In a series of 101 cases selected from a larger group of 243 patients with injury to the spinal cord, conus or cauda equina, only 1 patient (0.9 per cent)

TABLE 5 *Erd Results and Causes of Failure*

LEVEL AND TYPE OF INJURY	No. of Cases	24 Hour Bladder Control	CAUSE OF FAILURE											TOTAL FAILURES	STILL UNDER TREATMENT	TIDAL DRAINAGE NOT USED
			INEFFECTIVE THERAPY				MENTAL CHANGES			OTHER CAUSES						
			Ineffective Early Tidal Drainage	Associated Sepsis	Hypoproteinemia	Early Death	Senility	Idiocy	Psychosis	No Co-operation	Congenital Defect	Miliary Tuberculosis	Unknown (Tidal Drainage Effective)			
Cervical cord Physiologic transection	2	0	0	1	0	0	1	0	0	0	0	0	0	2	0	0
Nontransection	29	20	1	1	0	1	2	0	1	2	0	0	0	8	0	1
Dorsolumbar cord Anatomic transection	24	6	0	6	1	2	0	1	0	2	0	0	0	12	4	2
Physiologic transection	14	10	2	1	0	0	0	0	0	0	0	0	0	3	1	0
Nontransection	11	4	0	2	0	0	0	0	0	0	0	0	0	2	1	4
Sacral cord	9	4	0	2	0	0	0	0	1	1	0	0	1	4	0	1
Cauda equina	36	16	1	0	0	0	0	0	0	0	1	1	0	4	0	16
Totals	125	60	4	13	1	3	3	1	2	5	1	1	1	35	6	24

had had effective therapy, were free of associated infection, were neither senile, feeble minded nor psychopathic, would co-operate and were not still under treatment failed to have twenty-four-hour control of urination at the time of discharge. This end result was obtained only because of the efficient use of tidal drainage. The chances of securing this result were somewhat better (70 as opposed to 50 per cent) when tidal-drainage therapy was begun at the earliest possible moment after the injury. Transection of the cord below the first thoracic segment, whether anatomic or physiologic, does not of itself deprive the patient of this end result.

SUMMARY

Evidence is presented in support of the contention that every patient who has sustained an injury to

in whom tidal drainage was properly used for a sufficient length of time failed to have infallible twenty-four-hour control of urination at the time of discharge.

I am indebted to Dr. Augustus Riley, consulting surgeon for urology, Boston City Hospital, for his assistance with this work, much of which would have been impossible without his co-operation.

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healing and for a period of two weeks thereafter. At the end of this time tidal drainage can be begun, the bladder stretched to a useful capacity, and bladder training commenced in patients with transected cords after the bladder activity has become reflex or automatic. With such a background, neither the surgeon nor the patient need fear later suprapubic rupture when the bladder becomes distended.

Perineal Urethrostomy

Perineal urethrostomy need only be mentioned to be condemned. Its only advantage over suprapubic cystostomy is maintenance of drainage through the vesical sphincters. It accomplishes no more than does catheter drainage through the urethra and is as difficult to maintain under stress and with a shortage of attendants. In addition, it has all the risks that go with an open perineal wound. If it is maintained until the patient is ac-

The apparatus is difficult to clean, leaks develop easily in it, when full or nearly so it may overflow when the patient sits down, and it is useless when the patient is in bed. If the bladder is allowed to drain into it constantly, the critical level of fill, when associated with emptying of the reflex or "automatic" type, tends to decrease gradually until the bladder has so little capacity as to be useless as a reservoir. This is doubly true if the bladder is autonomous because of denervation. Proper bladder training in patients with a transected cord, supplemented in special instances by the use of a penile clamp and an inlying urethral catheter, with bladder irrigation at night by tidal drainage, will do all and more than a rubber urinal will do.

RESULTS

The results of treatment by tidal drainage as outlined above are summarized in Table 4. They are

TABLE 4 Twenty-Four-Hour Urinary Control at Discharge

TIME OF TIDAL DRAINAGE	NO OF CASES	COMPLETE CONTROL		COMPLETE CONTROL WITH TIDAL DRAINAGE		NO CONTROL		STILL UNDER TREATMENT	
		NO	PER-CENTAGE	NO	PER-CENTAGE	NO	PER-CENTAGE	NO	PER-CENTAGE
From the start	52	30	58	6	11.5	16	31	0	0
After an interval	49	22	45	3	6	19	38	5	10
Not used	24	19	79	0	0	5	21	0	0
Totals*	125	71		9	7	40	32	5	4
Averages		56							

tive, moreover, the tract is sealed off whenever the patient is seated.

Rubber Urinals

It is possible for a patient with injury to the spinal cord or cauda equina to remain dry and control the urinary outflow while active by wearing a rubber urinal strapped to his leg, provided that all the circumstances are favorable and that he is willing to sacrifice his bladder as a reservoir and to regard it only as a passageway for urinary flow between the ureters and urethra. Women will not wear these devices, however, because they are not consistently leakproof, and prefer absorbent pads. When worn by men they must fit exactly around the penis if they are not to leak. Since they are manufactured only in two sizes, — one for adults and one for children, — the matter of fit depends purely on chance. If it happens that a patient is able to fit himself properly, he must be prepared to forego the use of the urinal whenever edema of the perineal or penile skin develops and alters the fit. Inasmuch as irritation caused by the constant immersion of the penis in the fumes of stale urine during periods of activity is inevitable, the usefulness and efficiency of the apparatus proves to be considerably below the level envisioned by the patient and his physician at the time of its purchase.

given in terms of twenty-four-hour control of urination at the time of discharge from the clinic. Seven of the 9 patients who have control at home with the aid of tidal drainage are early cases, and today would be trained to do without this aid. The other 2 patients have denervated bladders and must use it. All 9 wear catheters constantly and have learned to clean and sterilize them and the apparatus and to remove and replace the catheter once a week in a sterile manner. One woman has been doing this for over nine years and has come to no harm. At night the patients attach their catheters to the tidal drainage setup, but during the day they are free of the apparatus and go about with the catheter clamped off, opening it only to allow the bladder to drain at three-hour or four-hour intervals. Three of these patients were subjected to an anterior dorsolumbar rhizotomy for the relief of a mass reflex,<sup>31</sup> 2 being the first ones on whom this operation was performed. Three others had functional transections, 1 had a demyelination of the cauda equina, and 2 have denervated bladders. Thus, 61 of 101 patients, including 38 with transections of the cord, have complete twenty-four-hour urinary control. Thirty-five have no control, and 5 are still under treatment.

Table 5 demonstrates that in 35 patients failure to attain twenty-four-hour control was caused by

The series consists of 21 cases of portal cirrhosis, with an additional case of possible arsenical cirrhosis as contrasted with so-called "alcoholic cirrhosis," 1 case of biliary cirrhosis and 2 cases of catarrhal jaundice in the acute phase (Table 1). Four peritoneoscopies, with biopsies in 3 cases, and a post-mortem examination have substantiated the clinical diagnoses. Four of the patients have died —

afebrile after treatment for specific infections. One patient (Case 7), in whom hemolytic *Staphylococcus aureus* was cultured from both the blood stream and the ascitic fluid, was treated with penicillin. Three patients (Cases 10, 11 and 15) were treated with sulfonamides for pneumonia.

Twenty-four patients showed no urinary sugar in the routine qualitative Benedict tests done on

TABLE 1 The Results of Intravenous Glucose-Tolerance Tests in 25 Patients with Liver Disease

CASE No	SEX	AGE	WEIGHT lb	CLINICAL DIAGNOSES	DEGREE OF LIVER DISEASE	BLOOD-GLUCOSE LEVELS		
						FASTING mg/100 cc	1 HR. mg/100 cc	2 HR. mg/100 cc
1	F	59	?	Portal cirrhosis serologic syphilis	Severe	97.5	119.6	73.1
2	M	43	164	Portal cirrhosis serologic and vascular syphilis	Severe	48.7	129.0	87.0
3	F	51	149	Portal cirrhosis cervical polyp	Severe	81.0	120.6	76.9
4	F	50	160	Cirrhosis possibly biliary	Severe	81.7	71.0	61.1
5	M	26	160	Catarrhal jaundice (infectious hepatitis)	Severe	74.4	113.6	67.3
6	M	64	127	Cirrhosis (possibly arsenical) serologic syphilis	Severe	53.0	172.0	72.0
7	M	54	200	Portal cirrhosis	Severe	97.4	114.2	103.3
8	M	64	183	Catarrhal jaundice (infectious hepatitis)	Severe	70.9	147.5	106.8
9	M	54	145	Portal cirrhosis Korsakoff's syndrome	Moderate	42.5	145.0	64.0
10	M	57	160	Portal cirrhosis	Moderate	74.1	114.8	64.3
11	M	56	178	Portal cirrhosis bronchopneumonia	Moderate	109.0	192.0	122.0
12	M	45	135	Portal cirrhosis	Severe	86.3	150.8	72.3
13	M	64	120	Portal cirrhosis	Moderate	77.6	155.0	98.0
14	M	64	171	Portal cirrhosis hypertrophic arthritis	Marked	53.0	107.0	63.0
15	F	47	154	Portal cirrhosis lobar pneumonia	Severe	75.4	107.5	83.7
16	M	63	178	Portal cirrhosis serologic syphilis	Severe	132.0	148.5	124.5
17	M	61	141	Portal cirrhosis	Severe	66.5	133.0	85.4
18	M	65	137	Portal cirrhosis serologic syphilis	Severe	81.7	132.5	95.3
19	M	67	179	Portal cirrhosis essential hypertension avitaminoses	Moderate	92.0	139.0	108.0
20	M	55	230	Portal cirrhosis tertiary syphilis	Severe	105.5	123.5	83.3
21	M	63	138	Portal cirrhosis	Severe	105.1	151.2	121.0
22	F	49	150	Portal cirrhosis	Severe	66.7	95.2	75.5
23	M	44	135	Portal cirrhosis	Severe	67.7	116.2	86.0
24	F	41	144	Portal cirrhosis	Severe	77.5	113.8	81.3
25	M	47	135	Portal cirrhosis	Severe	64.6	122.6	78.4

1 of bronchopneumonia, 1 of cardiac failure and 2 of hemorrhage from ruptured esophageal varices.

#### CLINICAL EVIDENCE OF LIVER DISEASE

Of the 25 patients studied, 15 gave histories of markedly elevated alcoholic intake, 8 were moderate drinkers, and 2 denied any use of alcoholic beverages. Thirteen patients gave dietary histories of food intake adequate in vitamin content as well as in caloric value.

The general nutritional status of these patients at the time the tests were performed was judged as good in 11 cases, fair in 4 and poor in 10. No patient, however, showed either marked obesity or emaciation.

Thirteen patients had occasional low-grade fever during hospitalization, 8 were afebrile, and 4 became

morning specimens. One (Case 11) frequently had a + to ++ test for sugar in the morning urine.

The significant physical and laboratory findings that were of aid in the general analysis of the extent and severity of the liver damage found in these cases are included in Tables 2 and 3. For purposes of tabulation, the various findings have been graded from 0 to ++++ to indicate the degree of abnormality found.

Hepatomegaly was demonstrated by palpation in all but 3 cases, and in these the ascites was so marked that adequate examination of the abdomen was impossible (Table 2). Palpable spleens were demonstrated in 7 cases. For both the liver and the spleen the degree of enlargement roughly corresponded to the number of fingerbreadths that the organ extended below the costal margin. Seventeen pa-

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## THE INTRAVENOUS GLUCOSE - TOLERANCE TEST IN LIVER DISEASE\*

JAMES A CAMPBELL, M D,† AND HENRY J TAGNON, M D ‡

BOSTON

THE liver plays an important role in the metabolism of carbohydrates. Clinical investigators have frequently reported observations of disturbed carbohydrate metabolism in the presence of liver disease,<sup>1-6</sup> and numerous studies have been made of the metabolic alterations found in experimental animals with liver damage induced either by toxic agents or by partial or total hepatectomy.<sup>7-9</sup>

The possibility that alteration of liver function enters into the production of the diabetic syndrome has been considered by many authors, and several reports have been published that emphasize the possible role of the liver in the etiology and pathogenesis of diabetes mellitus in human beings.

In 1939, Conn and Newburgh,<sup>10</sup> in an amplification of an earlier work,<sup>11</sup> reported their observations of glucose-tolerance curves in a series of obese patients. A majority of these patients were found to have curves of the so-called "diabetic type" following the oral administration of dextrose, and these were attributed to the excessive accumulation of fat in the liver. Conn et al.<sup>12</sup> and Coller and his co-workers<sup>13, 14</sup> reported the occurrence of such curves in patients with ascending infectious hepatitis. In their opinion, this abnormality was attributable to liver damage, and they reported a reversal of the abnormal curves to normal following

surgical treatment. In the above series, the tolerance curves were determined following the oral administration of glucose.

Soskin<sup>15, 16</sup> has repeatedly emphasized the role of the liver in the pathogenesis of diabetes mellitus both in experimental animals and in human beings. In 1935, he and Mirsky<sup>17</sup> observed abnormal oral glucose-tolerance curves of the diabetic type in certain patients with liver disease. Recently he and his co-workers<sup>18</sup> reported the cases of 6 diabetic patients whose conditions were aggravated by biliary infection. In 1943, he<sup>19</sup> published a preliminary report on abnormal curves obtained through intravenous dextrose-tolerance tests in patients with mild or early liver disease.

Many investigators have used oral glucose tolerance tests as a measure of liver function and have reported varying results.<sup>20-22</sup> The work reported herein was done in an attempt to determine whether there is an abnormality in carbohydrate metabolism as measured by an intravenous glucose-tolerance test, in patients with severe liver disease and to determine whether this procedure is a valid test of liver function.

### METHODS

The 25 cases from which the data in this report were obtained were studied as they appeared in the wards of the Boston City Hospital, with no attempt either to include or to exclude patients with diabetic tendencies. The only criterion for selection was clinical and laboratory evidence of marked liver damage at the time the glucose-tolerance tests were performed.

\*From the Thorndike Memorial Laboratory the Second and Fourth (Harvard) Medical Services Boston City Hospital and the Department of Medicine, Harvard Medical School.

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†Teaching fellow in medicine Harvard Medical School resident Fourth Medical Service Boston City Hospital.

‡Instructor and Francis Weld Peabody Fellow in Medicine, Harvard Medical School, tutor in biochemical sciences Harvard University, assistant in medicine Boston City Hospital.

and Maddock<sup>26</sup> All such tests are standard procedures The normal range of values, as well as differences to the method used in the various determinations, are included in the table

Gradation of the extent of liver damage as shown by the liver-function tests was from 0 to ++++ If 80 per cent or more of the tests performed gave abnormal results, the case was graded as ++++,

obtained by them has been incorporated in Figure 1 In the same report they tabulated observations in a number of patients with known or suspected disease The findings in the present study are consistent with those reported in Lozner's series for a group of 7 patients with liver disease

To be considered abnormal, a value should differ from the normal mean value by an amount greater

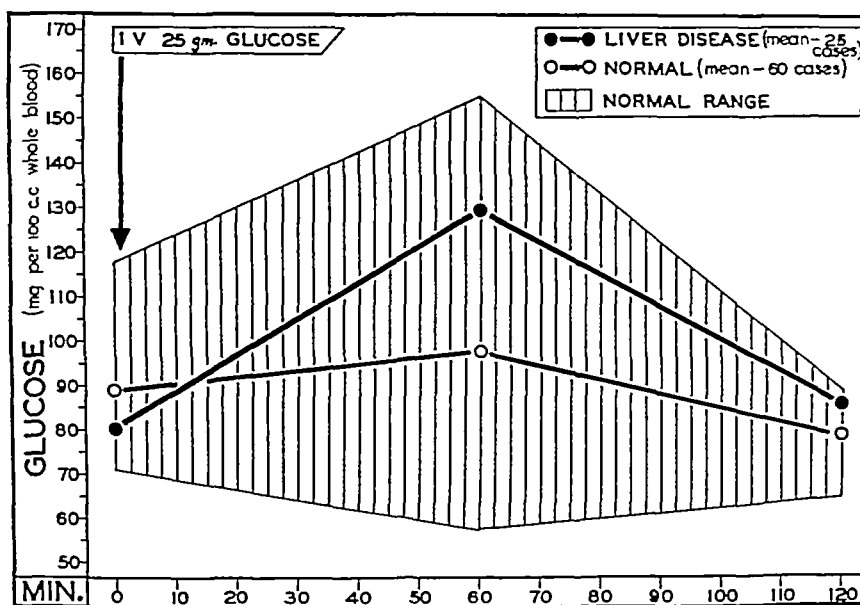


FIGURE 1 Intra-venous Glucose-Tolerance Curve in Liver Disease

if 65 to 80 per cent of the tests did so, it was graded +++, and if 45 to 65 per cent did so, it was graded as ++

In addition, an intravenous glucose-tolerance test as described by Lozner, Winkler, Taylor and Peters<sup>37</sup> in 1941 was carried out in these patients Urine samples collected during the test were analyzed for glucose by the quantitative method of Benedict<sup>38</sup>

A total evaluation of the severity of the liver disease was determined by consideration of the clinical findings, the laboratory evidence of abnormal liver function and the course The disease was considered moderate in 5 cases, marked in 1, and severe in 19 No mild cases were encountered

## RESULTS

The original data are presented in Table 1 The form of the curve derived from these data relating blood-glucose values to time is indicated by the heavy black line in Figure 1 The individual curves varied considerably, but the average curve fell within the range in normal subjects There were marked differences in blood-glucose levels at each of the three time intervals, with the least degree of variation, as well as the minimum standard deviation, occurring at the two-hour interval (Table 4) This is in accord with the findings in 60 normal subjects on whom this test was performed by Lozner and his co-workers,<sup>37</sup> and an analysis of the curves

than three times the standard deviation of the mean

For further analysis of the results obtained in the present study, the cases were divided into the following groups, as suggested by Lozner et al<sup>37</sup> Group A, those with blood-sugar concentrations, two hours after the injection, within the normal range, from 65 to 99 mg per 100 cc, Group B, those with moderate elevation of the blood sugar, ranging between 100 and 119 mg, Group C, those with markedly elevated blood sugar, ranging between

TABLE 4 Summary of Results of Intravenous Glucose-Tolerance Tests

BLOOD SPECIMEN	BLOOD-GLUCOSE LEVELS			
	MAXIMUM	MINIMUM	ARITHMETICAL MEAN	STANDARD DEVIATION
	mg/100 cc	mg/100 cc	mg/100 cc	mg/100 cc
Fasting	132.0	42.5	81.2	20.1
One hour after injection	192.0	71.0	129.2	25.4
Two hours after injection	124.5	61.1	85.7	18.9

120 and 160 mg, and Group D, those with the blood sugar moderately depressed, ranging from 38 to 64 mg The values in Group A differ from the normal mean established by Lozner by less than three times its standard deviation those in Group B by more than three but less than six times, and those in Group C by more than six times The results are presented in Table 5

Four cases (Cases 7, 8, 19 and 21) were placed in Group B Three of these were cases of portal

tients had ascites, and in 13 of these paracenteses were performed. The cases in which repeated taps were necessary or in which 5000 cc or more of fluid was withdrawn were graded as + + + +. Those re-

significance has been assigned by some physicians,<sup>2</sup> were found in 11 cases.

A grade of + + + +, indicating the extent of development of collateral circulation found in throm-

TABLE 2 Clinical Findings

CASE No	HEPATOMEGALY	SPLENOMEGALY	ASCITES	PERIPHERAL EDEMA	SPIDER ANGIOMAS	COLLATERAL VEINS	HEMOGLOBIN (SALT)
1							%
2	+++*	?	++++	++++	+++	++	70
3	++++*	0	++++	++	+	++	61
4	++++	0	++	++	+	++	38
5	++++	0	0	0	0	0	70
6	++++	0	++	++	0	++	96
7	++++	+	++++	0	0	++	83
8	++++	0	++	0	0	++	69
9	++++	0	0	0	0	0	92
10	++++	0	0	0	0	0	83
11	++++	+	0	0	0	0	83
12	++	+	++	++	++	++	88
13	++	0	0	0	0	0	77
14	++	0	0	0	+	+	87
15	++++	+	+	+	++	++	85
16	++++	+++	++	++	0	++	61
17	++++	0	++	++	0	0	56
18	++*	?	++	++	0	++	73
19	+	+	++	++	0	++	65
20	++++*	?	++	++	+	++	70
21	++*	?	++	++	0	++	73
22	++	0	++	++	0	++	64
23	++	0	++	0	0	++	70
24	++	0	++	0	0	++	67
25	++	0	++	0	+	++	44
							55

\*Liver and spleen masked by ascitic fluid

quiring a single tap in which less fluid was removed were graded as + + +, and those in which there were physical signs of fluid but in which paracentesis was not necessary were graded as + + or +. The patient in Case 7 had paracenteses for relief of extremely painful abdominal distention and increasing dyspnea on an average of once every two weeks.

hepatic damage, was assigned to only 2 patients, both of whom died from ruptured esophageal varices.

#### LABORATORY EVIDENCE OF LIVER DISEASE

The results of the liver-function tests performed on these patients are recorded in Table 3. Reviews

TABLE 3 Laboratory Tests

CASE No	ICTERIC INDEX <sup>27</sup>	URINE URO-BILINOGEN <sup>28</sup>	CEPHALIN FLOCCULATION <sup>29</sup>	BILE IN URINE (FOAM TEST)	FORMOL GEL <sup>30</sup>	TOTAL PLASMA PROTEIN <sup>31</sup>	PRO THROMBIN TIME COMPARED WITH NORMAL <sup>32,33</sup>	HIPPURIC ACID EXCRETION <sup>34</sup>	15 MINUTE RETENTION OF BROM SULFALFALIN <sup>35</sup>	ALKALINE PHOSPHATASE <sup>36</sup>	
	Normal	0-10	1-8-1 32	0-+	0	0-++	gm /100 cc 5 80-7 90	% 80-100	gm /4 hr 2 7 or more	% 10 or less	units 6 or less
1		35	1 64	++++	++	-	4 82	52	-	-	1 26
2		35	1 32	++++	+	-	4 89	60	2 40	-	5 03
3		50	1 64	++++	++	++++	5 38	75	-	90	18 31
4		50	1 128	++++	++	++++	5 41	100	-	-	5 20
5		100	1 64	++++	++	++++	5 75	100	-	-	-
6		35	1 64	++++	+	++++	6 05	100	1 20	40	1 90
7		12	1 16	++++	-	++++	5 72	60	1 80	20	6 40
8		50	1 64	++++	++	++++	5 78	100	-	-	-
9		75	1 256	++	-	-	4 82	90	2 30	15	2 90
10		10	1 32	+	-	++++	5 32	80	0 88	10	7 66
11		75	1 64	++++	+	++	5 88	80	1 70	-	-
12		50	1 64	++++	++	++++	4 66	70	0 69	20	-
13		15	1 32	++++	-	0	5 09	50	-	-	4 37
14		75	1 64	++++	-	-	5 78	-	-	30	-
15		22	1 128	++++	-	-	5 02	35	2 20	40	-
16		35	1 256	++++	+	++++	5 16	52	0 80	60	-
17		35	1 256	++++	++	++++	5 60	50	-	60	3 37
18		15	1 4	++++	-	0	5 86	68	-	-	-
19		5	1 8	++	-	++	5 70	52	1 16	10	-
20		75	1 64	++++	++	-	6 25	-	1 63	-	9 04
21		5	1 32	++++	+	++	5 21	70	1 80	10	5 90
22		33	1 256	++++	++	++++	5 26	100	-	-	3 29
23		25	1 8	++++	++	++++	5 67	100	2 04	-	3 56
24		25	1 128	++++	++	++++	5 63	100	-	-	4 03
25		10	1 32	++++	+	++	4 52	75	0 75	60	-

\*Sodium benzoate (5.9 gm) given orally

†Bromsulfalein (2 mg) injected intravenously

over a period of fourteen months, and each tap yielded between 18 and 20 liters of fluid.

Spider angiomas, to which such grave prognostic

of the evaluation of various such tests have recently been published by Quick,<sup>24</sup> Mateer and his co-workers<sup>25</sup> and, from this hospital, by White, Deutsch

No diagnostic value could be assigned to the tests in this series as an index either to liver function or to disturbed carbohydrate metabolism

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cirrhosis, 2 of them with severe liver damage. None of the individual curves were remarkable in contour, however, or suggestive of the diabetic type of curve.

Two cases (Cases 11 and 16) were placed in Group C. Both patients had portal cirrhosis, one with severe and the other with moderate liver damage.

Included in the cases with moderate depression in the blood-sugar concentration are 3 of cirrhosis of the portal type and the single case of biliary cirrhosis in the series. By far the greatest portion of the cases with liver disease, however, were in the

TABLE 5 *Analysis of Distribution of Cases according to Blood-Glucose Levels in Fasting Specimens and Those Taken Two Hours after the Injection of Glucose*

GROUP	BLOOD-SUGAR LEVEL	
	FASTING	AFTER INJECTION
A (normal)	17	15
B (moderately elevated)	3	4
C (markedly elevated)	1	2
D (moderately depressed)	4	4

group showing normal blood-sugar values, both in the fasting state and two hours after the test glucose injection. This group includes 1 case of severe acute hepatitis, in addition to the cases of chronic liver disease.

Of Lozner's group of 60 normal persons, all except 1 showed glycosuria during the intravenous glucose-tolerance test, with a maximum amount of glucose excreted by any subject of 2.25 gm. In the present study, the patients exhibited glycosuria during the test in all cases except 2. The maximum total urinary glucose excreted in any one case was 2.50 gm, with an average total of 0.67 gm, showing no appreciable deviation from the normal.

### DISCUSSION

Newburgh and Conn,<sup>10, 11</sup> in discussing their observation of diabetic-type glucose-tolerance curves in obese patients, suggest that this occurrence depends on the excessive accumulation of fat in the livers of obese patients, with resultant impairment of hepatic capacity to store glycogen. No pathologic evidence in support of these claims was offered, however, and it is known that fatty infiltration of the liver does not preclude glycogen storage<sup>39</sup> and that it not infrequently occurs in Von Gierke's disease.<sup>40</sup> In these authors' cases of ascending infectious hepatitis,<sup>12</sup> as well as those of Coller,<sup>13, 14</sup> in which diabetic-type glucose-tolerance curves were observed, the extent of the liver damage was not completely evaluated, the pathological data reported were not markedly abnormal, and the glycogen studies done on tissue removed at the time of operation were entirely within normal limits. All these studies were made by using the oral administration test method.

Soskin<sup>15</sup> has shown that a diabetic type glucose-

tolerance curve can be obtained in completely hepatectomized dogs. It is obvious that a similar situation is never encountered in man, and the data presented here indicate that the extent of liver damage compatible with life is not sufficient in human beings to cause a marked alteration of the glucose-tolerance curve after intravenous injection of glucose. Indeed, the regulation of the blood sugar, as measured by such a test in the cases reported here, seems to be by far the best preserved of all liver functions.

In the 6 diabetic patients whom Soskin et al<sup>15</sup> reported as showing increased metabolic disturbances with the development of liver disease, the initial function studies performed failed to demonstrate much evidence of liver damage, and repetition of the tests after therapy was not frequent enough to evaluate accurately any changes that may have occurred. No studies to determine liver function were reported in any of the patients who showed aggravation of their diabetic condition following therapy for liver disease, nor was any explanation offered for their relapses.

In Soskin's<sup>15</sup> preliminary report on the intravenous glucose-tolerance test in patients with liver disease, his findings in such cases were interpreted as showing definitely abnormal curves with a characteristic contour, and the possible use of the test as a diagnostic aid in cases of early or mild liver disease was thus suggested. Until the detailed data from which Soskin's results were obtained are available for statistical analysis, however, no accurate conclusions can be drawn.

The advantages of the intravenous as compared with the oral glucose-tolerance test are manifold.<sup>41, 42</sup> In addition to obviating any anorexia or nausea that may prevent proper ingestion of the test sugar, an intravenous test automatically removes such important variables as gastric motility and intestinal absorption in a test of glucose tolerance in any subject. The significance of the latter factor is well demonstrated in comparing the oral with the intravenous curves in a case of steatorrhea.<sup>37</sup> It seems particularly necessary to consider these advantages in studying cases of liver disease in which stasis in the portal circulation and delayed absorption from the gastrointestinal tract may conceivably cause the protracted periods of hyperglycemia following oral administration of glucose that have been reported in the literature.

### SUMMARY AND CONCLUSIONS

An intravenous glucose-tolerance test was performed on 25 patients with liver disease, each of whom showed by clinical and laboratory examinations evidence of severe to moderate liver damage at the time the test was performed.

Although extreme variations appeared in individual tests, by far the greater proportion of the values obtained were within normal range.

ally selected as to its length, so that when the curve of the clavicle was taken into account the nail would be sufficiently long to engage the inner fragment. This nail, made of stainless steel, was placed in the drill hole and driven through the

By May 17, the wound was well healed. Roentgenograms taken at that time showed satisfactory alignment of the fragments and evidence of union (Fig. 3). On June 14, the nail was easily removed through a 2-cm incision under local



FIGURE 2 Roentgenogram Showing Complete Fracture in the Outer Half of the Clavicle, with Displacement of the Fragments

medullary area of the outer fragment into the inner fragment. It was driven in completely, so that its head did not protrude. The forceps were removed, and the wound was closed in the usual manner and without drainage. The skin was closed

anesthesia. A roentgenogram showed solid union (Fig. 4). A perfect anatomic and functional result was achieved.

The idea of using a nail in handling fractures of the clavicle is not new, although few such cases have



FIGURE 3 Roentgenogram Taken Two and a Half Weeks after Operative Fixation, Showing Good Alignment of the Fragments and Evidence of Union

with endermic sutures. No retentive dressing or apparatus, not even a sling, was applied. In 4 days, the patient was discharged from the hospital. Motion was possible as soon as the traumatic reaction had subsided.

been reported. Lambotte<sup>1</sup> recommended the use of a screw or longitudinal nail in transverse or slightly oblique fractures and reported sixteen such opera-

## CLINICAL NOTE

## TREATMENT OF FRACTURE OF THE CLAVICLE BY INTERNAL NAIL FIXATION\*

REPORT OF A CASE

HAROLD G LEE, M.D.†

BOSTON

**F**RACTURES of the clavicle can almost invariably be satisfactorily treated by conservative measures. The fragments unite easily and quickly, and the functional results are good, even though there may be a certain amount of residual deformity and shortening of the clavicle. In an occasional case of fracture of the outer end of the bone in which it is desirable to obtain perfect alignment and retention

operative technic with intramedullary nail fixation was successfully accomplished. It is understood that surgery of this type is not without its dangers and should be undertaken only by a qualified surgeon.

The problem presented by the fracture that lies in the outer half of the clavicle is similar to that of an acromioclavicular dislocation. The shoulder with the distal fragment is tilted downward, and the proximal fragment rides upward. In certain cases it is difficult to approximate the fragments and hold them in position. If the anatomic alignment is not maintained, the distal fragment tends to slip back and forth, carrying the periosteum down under the clavicle. Herein lies a potential danger in that a bony spur may develop under the clavicle (Fig 1).

## CASE REPORT

A V, a 23-year-old man, was admitted to the hospital on April 29, 1943, complaining that the left shoulder had "let go" when struck by a baseball. The roentgenographic examination showed a complete fracture in the outer half of



FIGURE 1 Roentgenogram Showing a Bony Spur That Developed under the Clavicle following Failure to Maintain Alignment of the Fragments after Reduction

of the fragments, the usual closed methods of treatment are inadequate. In such fractures, intramedullary fixation of the fragments by Kirschner wire has been carried out with success, but its use is not without danger, as is attested by several fatalities that have resulted from penetration of nearby arteries. In the case here presented, an

the clavicle, with the distal fragment tilted downward (Fig 2). Repeated attempts at closed reduction and retention of the fragments failed.

Operative intervention was carried out as follows. Under general anesthesia, a posterior incision running longitudinally to the axis of the bone and above its curve was made at the outer end of the clavicle. The fragments were exposed and their ends cleaned. The fragments were approximated, and bone forceps were applied to hold them in position while a nail was being introduced.

A drill hole was made in the outer end of the clavicle after the point of entrance for the drill had been calculated by studying the position of the fracture. The nail was care

\*From the MacAusland Orthopaedic Clinic.  
†Orthopedic surgeon, Carney Hospital.

## SYMPOSIUM ON MEDICAL SOCIOLOGY

### THE POINT OF VIEW OF ORGANIZED MEDICINE TOWARD THE DISTRIBUTION OF MEDICAL CARE\*

LOUIS H. BAUER, M.D.†

THE problem to be discussed is that of medical care. It is a controversial issue, in fact, if it were not so there would be no problem. I should like to appeal for a sound and sane method of approaching it. It is a problem that is comparatively recent, having developed within the last two decades. It has been brought about by the increased costs of medical care.

One of the reasons for this situation has been the increased cost of medical education, but the chief one has been the increased cost in diagnosis. After all, the physician giving the medical care receives little more money than he did a good many years ago, but the cost of arriving at the diagnosis is tremendously greater, and the result has been that there are certain persons who find it difficult to meet the economic burden of illness, particularly prolonged or so-called "catastrophic" illness. More persons go to hospitals and more have private nurses, and both these trends increase the cost of medical care.

There has been a great deal of propaganda concerning the distribution of medical care in the United States, and not all of it is well justified. For example, a so-called "National Health Survey" was conducted in 1939, as the result of which it was stated that one third of the people of the United States were without medical care. This statement is certainly not true today, and I do not believe that it ever was true. The figures were based on a survey of what was not a true cross-section of the country but a cross-section of a certain area, held in an effort to unearth chronic sickness. No effort was made to find out *why* people did not receive medical care. The survey was carried on by 6000 W.P.A. workers of high-school age who had no training whatever in what they were to do or in how to do it. I daresay that at least a third of those present did not have medical care in 1944. I did not have any myself, but it certainly was not because I could not get it. It must be remembered that many persons are not ill. Others prefer to secure medical care through patent medicines bought in drugstores. Others go to cultists, osteopaths or chiropractors, and still others, such as Christian Scientists, have religious scruples against accepting medical care. All these things must be taken into consideration.

Even the survey mentioned revealed that 17 per cent of persons with incomes of over \$3000 did not have medical care. Certainly, the economic factor was not the important one there.

Shortly after the results of this survey were published, the Medical Society of the State of New Jersey, by means of the radio, the press and public speakers, stated that anyone in that state who could not get medical care should immediately apply to the medical society and promised that care would be given them. Of a population of over 2,000,000, only 7 persons reported that they could not get medical care, and none of them were actually unable to do so. They simply did not know how to go about it.

The statement frequently made is that half the counties in the United States are without a general hospital. This is true, but it is not stated that of these thirteen hundred counties only thirteen are more than thirty miles from a general hospital. With good roads thirty miles is not a great distance to transport a patient. In fact, it is often easier to transport a patient twenty or thirty miles in a rural district than it is to take him five or ten miles to a city with its traffic problem. Nor is it stated that of these thirteen counties only 5 have a population of more than 5 persons per square mile.

The United States has the lowest death rate of any country in the world except New Zealand, and New Zealand can hardly be compared with the United States concerning either the character of its population or its medical problems. The rate of the United States has constantly decreased, and even during World War II, with the shortage of physicians and nurses, death rates remained surprisingly low, and those in many areas even decreased. The life expectancy has increased forty years in as many years. Infant mortality has dropped 50 per cent since 1920.

Draft statistics are often cited as showing that the American public is gradually falling apart physically. The facts are that approximately 4,000,000 men were rejected in the draft, and that of these, 800,000 were illiterate. Nearly 800,000 more were rejected because of neuropsychiatric defects. It is questionable how much medical care or lack of it had to do with the development of these conditions. Nearly 1,000,000 men were rejected on account of bad teeth, but most of them were later accepted. Between 200,000 and 400,000 men had remediable defects. A great many of these men could

\*This is the seventh of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March 1945. They were sponsored by the Department of Preventive Medicine and were primarily intended for third-year students. These articles will temporarily replace the reports "Medical Progress."

†Member, Board of Trustees, American Medical Association.

tive fixations. In all except one, the patient recovered good function and the fragments were perfectly aligned. Osteosynthesis by a nail was also proposed by Spitzzy,<sup>2</sup> Bonnet<sup>3</sup> and Johnson.<sup>4</sup>

It has been customary to consider some form of postoperative external splinting as necessary for adequate fixation, regardless of the type of osteosynthesis, but in following the nail fixation in the

removed as soon as the roentgenogram shows solid union.

#### SUMMARY

A case is presented of a fracture in the outer half of the clavicle in which operative intervention and fixation by means of a nail were satisfactorily carried out. No postoperative dressing or splint was re-



FIGURE 4. Roentgenogram, Taken Six and a Half Weeks after Operative Fixation, Showing Solid Union.

present case, no external retentive dressing, not even a sling, was required.

One objection to nail fixation of fractures of the clavicle is based on the possibility of ulceration of the skin from the head of the nail. In the method herein described, the head lies in the posterior aspect of the clavicle, so that the skin is not pulled over it. Another objection is the danger of irritation of the bone, giving rise in some cases to osteitis and in others to hypertrophied callus. This danger is not encountered with this technic, because the nail is

removed. The method afforded complete comfort to the patient and permitted him to be ambulant, thereby definitely curtailing the period of incapacity.

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prevent the rendering of a mere quantity of medical care rather than care of a high quality. In the development of any new type of insurance, it takes time to make it successful and acceptable. At present all sorts of voluntary insurance plans are under experimentation. Some of the industrial plans date back twenty years, but many of them are of extremely recent origin. Many such plans have been started by medical societies have altered their method of coverage. Some of them have failed simply because they were not on a sound actuarial basis and were not organized to deliver good medical care.

When the problem of insurance first came up, no one knew just what should be done. There was no actuarial background for any of these plans. No one knew how the public would react to the proposition or how physicians would react to it. Consequently, there was blind groping, but during the last four or five years a good deal of experience has accumulated showing some things that are good and some that are not.

The American Medical Association has been severely condemned for not proposing a voluntary plan to cover the whole United States. To my mind, this would have been the surest way of killing the whole thing, for the very reasons just stated. No one was in a position to say what the best type of plan would be, and even now we are not entirely sure. It is my opinion that there never will be a single plan that is satisfactory for the whole United States, because a plan that will work in Missouri and Arkansas may not work in Massachusetts, what will work in the city will not work in the country, and what will work in agriculture will not necessarily work in industry. So that a variety of plans are needed, and I think that this will be the answer so far as insurance is concerned.

There are persons who say that the voluntary plans will not work. Such statements are made in haste and perhaps maliciously — those who make them do not want voluntary plans to succeed because they prefer compulsory ones. Nevertheless, group hospital insurance, which is one form of voluntary insurance, has grown tremendously in the last few years. There are now over 19,000,000 persons in the United States who are covered by it. This is admittedly not enough, but in view of the increasing demand for this type of insurance, there is no reason why it should not be made available on a country-wide basis, and it probably will be. There are over 25,000,000 other persons who are covered, at least to some degree, by voluntary nonprofit medical-society plans, industrial plans and commercial plans. These plans vary from complete medical coverage to coverage only for surgery and obstetrics, and from coverage for the whole family to that for workmen only.

These plans must be made available to everyone who desires to be insured, and at a cost within his

means to pay. Over half the states in the Union now have nonprofit plans, either in operation or in the throes of organization. Growth has been slow and will continue to be so, but it has been much more rapid in the last two or three years than anyone thought possible at the beginning. The public is not yet sold on the idea. There have been all sorts of surveys. They disagree on some points, but they all agree that the public is demanding some method of prepaying its costs for catastrophic illnesses, and the majority of the surveys state that the public prefers to do this on a voluntary basis if it can be so arranged. The American Medical Association is about to appoint a director of insurance to correlate these types of plans and to stimulate their growth. The only reason it has not been done already is that the proper man for the job has not been found, but he soon will be.

It has been suggested that the indigent could be covered by having the state or county or town concerned purchase voluntary policies instead of hiring a so-called "poor" physician or paying the physicians' bills directly.

The Committee on Public Relations and Economics of the Medical Society of the State of New York states that 2 to 10 cents a day per person will adequately cover both medical indemnity and hospital insurance, that a broad surgical contract costs 2 cents a day per person, that a surgical contract including obstetric care costs \$1.70 a month per family, and that a liberal medical and surgical contract with obstetric care costs \$3.00 a month for an entire family. Such plans are available in certain areas, but they have not yet been made widely enough available, and we are trying to see that they are.

I have said that there are some persons who contend that voluntary insurance will not work, but it has not been tried long enough for them to make any such statement. One of the reasons given is that such insurance did not work in Europe. This is an unfair comparison, because in this country no voluntary plan that is worth anything has the slightest relation to any of the so-called "lodge practices" or "friendly societies" in Europe prior to the adoption of the compulsory program.

As already stated, insurance is only one answer to the problem. Adequate diagnostic facilities must be available in every area. If the local communities are not able to support diagnostic centers, they must get subsidies from the state. If neither the local community nor the state can finance them, the federal government must do so. If diagnostic facilities are available at reasonable cost, and there is voluntary insurance as well, the problem of the cost of medical care will be largely solved.

It has been publicly stated that the American Medical Association is against this program, as it was against those proposed in 1928, 1932 and 1934, but there is scarcely anyone whose opinion has not

have been cured and entered the service, but they refused to do anything in that direction.

A great many men were rejected on account of defective eyesight. Here again, it is doubtful whether any amount of medical care would develop good eyesight. Many of these men might not have had such poor eyesight if they had been instructed in the proper care of their eyes in their early days, and the same thing applies to those rejected for poor teeth. Proper knowledge of dental hygiene might have saved a great many of them but the figures would probably not have been materially affected by an increase in medical care.

During the 1939 survey, a prominent weekly magazine published a cartoon showing a hut on the side of a hill, — it was nothing more or less than a few boards nailed together, — with an emaciated woman in rags, accompanied by two or three children, all practically naked. The cartoon was entitled, "These people need medical care." They did need medical care, but they needed some other things a great deal more. They needed a proper place to live and proper food and clothes. Had they had these, they would not have needed so much medical care.

I do not wish to give the impression that I think that all is well with the status of the medical care in the United States, because I do not. It needs a great deal of improvement. Owing to increased costs there are persons who cannot afford good medical care, and there are others who stay away from physicians rather than accept charity. This situation must be remedied.

The difference in opinion that exists relates to the manner in which the situation should be remedied. First of all, it must be borne in mind that there are certain areas in the United States in which good medical care simply is not available, because the area is such that it cannot support a physician or a hospital. If a physician takes up practice there, he either soon goes somewhere else because he cannot practice good medicine, or — what is even worse — stays there and practices poor medicine.

It is thus evident that the lack of proper diagnostic facilities in certain areas of the country must be remedied. There is probably no one in Massachusetts who is unable to get medical care, and this is certainly so in New York State, but not all states are so well favored.

There is also a serious lack of facilities for preventive medicine in the United States. About half the counties have no county health department. It is not necessary for every county to have such a department, but every district should have one. In sparsely settled areas, two or three counties may combine to have a district health center.

There are four economic groups in the United States. The first comprises those who are financially well enough off to meet any conceivable situation. The second includes those who can meet the ordinary

costs of living and ordinary medical expenses, but find it difficult to meet those of long and expensive illness. In the third group are those who can meet the costs of the bare necessities of life but cannot meet the costs of any sickness. The fourth group comprises those who are dependent on public aid for housing, clothing and nutrition as well as for medical care.

The first and last groups require little consideration. Those in the first group can afford any type of medical care that they desire. Those in the last group in most areas are likewise well taken care of through charity hospitals and welfare departments. There are certain areas in the country in which this is not true, and that situation must of course be remedied. The other two groups are the ones that cause the most concern, being comprised primarily of those in the middle income bracket. What is the best way to meet this need? The American Medical Association believes that medical care of a high quality should be available for every person in the United States. The difference of opinion relates to how this medical care should be distributed.

Those of you who are on the faculty will recall that many changes have occurred in the therapeutics of certain diseases. They remember, as I do, the time when there was no treatment of pneumonia except bed rest and fresh air. I remember a remark made by Dr. Frederick Shattuck, our professor of medicine, to the effect that if he had pneumonia he would want to be in bed in a room with the windows open and a fire in the fireplace and to have someone feed him plenty of liquor. This, he said, was about the best treatment there was for pneumonia. Then serum was developed. It was not adopted immediately, and even after considerable experimentation it was used only gingerly. In fact, for a long time there was serum only for certain types of pneumonia. Somewhat later, the sulfonamide drugs came on the market, but physicians did not abandon the use of serum. Both were employed, and only recently has serum gone more or less into the discard. Next came penicillin, but the sulfonamides have not been given up because of it. A new system of therapeutics in the treatment of pneumonia has gradually evolved over a prolonged period. Perhaps ten years from now all these methods will be in the discard and there will be something else.

The same approach should be made to the problem of distribution of medical care. Since our nation has been made the healthiest in the world through private enterprise, why should this be abandoned for something different? Let us experiment gradually, testing various plans that have been suggested.

The medical profession has accepted the principle of insurance as one of great assistance, but it continues to believe that such insurance should be on a voluntary basis to avoid political interference and

ise reach the unemployed class, so that it still does not solve the problem of the indigent. Finally, it is inordinately expensive, and results in a tremendous bureaucracy, with the accompanying red tape and inefficiency. Voluntary insurance, on the other hand, gives either a cash indemnity or medical service that the patient can use when and where he wants it. The physician is responsible to him and not to a bureaucrat.

The most outstanding example of compulsory sickness insurance that has yet been suggested in this country is that proposed by the Wagner-Murray-Dingell Bill, which died in the last Congress but has been reintroduced by Congressman Dingell.\* It has not been reintroduced in the Senate. This is an extension of the Social Security program, which is in vogue in this country at the present time. Certain Social Security provisions of this bill have already become law, such as old-age security and unemployment insurance. There are some persons who are against this trend and think that we have gone too far, but this is an idle argument. Social security is here whether we like it or not. It is going to stay and we might as well accept the principle of it. The Wagner-Murray-Dingell Bill, however, goes farther and attempts to put compulsory sickness insurance into effect throughout the country. In substance, this bill would extend social security coverage to at least 110,000,000 persons in the United States. It would deduct 6 per cent from the employee's pay up to \$3000, and the employer would contribute an equal amount — a total payroll tax of 12 per cent. Self-employed persons would pay 7 per cent up to \$3000. In times of full employment this tax would bring in something over \$12,000,000,000 a year.

Not all this, of course, is for medical care. It is estimated that 25 per cent of the total income would be earmarked for medical care, or something over \$3,000,000,000 a year.

Senator Murray has stated that there will be no politics in the handling of this money. I hope that he is right, but I am extremely skeptical about it. It would certainly shatter most precedents. This does not mean that because there are public funds there must be politics. Locally, this is less likely to occur, since the people are much closer to those who are administering the program and stand guard over it. When, however, federal funds are controlled by the federal government for a project that may be three thousand miles away, politics is bound to come in, because there are many middlemen, and a tremendous bureaucracy is built up. In Germany, before the war, there were more people working in the Health Bureau than there were physicians working for it.

This bill places full authority for administration

in the hands of the Surgeon General of the United States Public Health Service, under the Social Security Board. It provides for an advisory council of sixteen who will be appointed by the Surgeon General from lists of nominees submitted by the various professional and other organizations. Presumably there would be physicians on this panel but there is not a single word in the bill to the effect that there *must* be a physician on the council. As a matter of fact, this makes little difference, because the council will have no authority. All it can do is to give advice, which may or may not be taken.

The bill provides for so-called "free choice" of physician, but this means free choice provided that the physician agrees to take part in it. In England, the majority of the better physicians refuse to play any part in the compulsory sickness-insurance scheme.

The bill also prescribes how and under what conditions the physician may participate. It provides for three possible methods of payment — a fee for service, a full-time or part-time salary or payment on a per capita basis.

The Surgeon General may limit the number of patients a physician may treat and under certain conditions he may arbitrarily assign patients to a particular physician. He sets up the standards for specialists and determines who meet them, and the patient has no choice whatever in the selection of a specialist. He is authorized to determine what hospitals can take part in the program, and within the limits prescribed in the bill can determine what those hospitals will be paid. It is my opinion that limitation of payment to the amounts set forth in the bill would result in the closing of most of the voluntary and private hospitals in the country or their conversion to government control.

There is provision for certain laboratory and hospital benefits, the nature and extent of which are to be determined by the Surgeon General. The bill also provides for grants-in-aid for medical education and research, with the result that the Government will eventually control both.

American medicine has been responsible for a state of health of the people unexcelled in any other country. The enactment of this bill would result in its deterioration, for if medical education suffers, if the quality of medical care becomes attenuated and if the incentive to individual medical research is removed, the resulting harmful effect on the health of the people is inescapable. Another tremendous bureaucracy will grow up.

Another point, which has been brought out by the American Bar Association is that neither the patient nor the physician will have any recourse from regulations or decisions issued by the Surgeon General, who is not an elective but an appointive official, except to a board appointed by the authority who wrote the regulations and made the decisions. One cannot appeal even to the courts.

\*These paragraphs apply to the previous version of the Wagner-Murray-Dingell Bill. The present bill (S 1606) makes no mention of taxes and does provide for court action. The principles of the two bills are the same.



changed in the course of years on various problems of the day. Even as late as the summer of 1941, a large part of the population of the United States were against this country's entering the war, but it would be hard to find any red-blooded citizens who are not wholeheartedly for war now. Ideas have changed. The whole question of medical insurance was hazy twenty-five years ago. There was not the need for it then that there is now. Naturally, the American Medical Association did not sponsor any such program when the need for it was not shown.

Another piece of propaganda that is often leveled at the American Medical Association is that it is against group practice. There is a prominent doctor in Boston, a president of the American Medical Association only two or three years ago, who is head of one of the outstanding groups in the United States. Both the Mayo brothers served as president of the Association. There is a member of the Mayo Clinic who is a member of the Board of Trustees of the Association, and other examples could be cited. The American Medical Association is, however, against groups that are organized purely for profit and not to deliver a good grade of medical care, but groups as such have not been frowned on. Many such groups started after the last war, but they failed, not because of any disapproval of organized medicine but because the public could not support them. The public likes Dr. Smith but it does not like Dr. Brown, and patients will go to Dr. A but not to Dr. B.

Another point that should again be stressed is that of adequate health supervision in the way of preventive medicine for every district in the United States. There again, federal funds may be used to help subsidize the local communities that are unable to support such facilities.

For the last seventy years the American Medical Association has asked for a United States Department of Health, with a cabinet officer in charge and with the same status as all the other cabinet departments in the government. This request has never been granted, and this may not be the time to push such a proposition, because the present trend is to carry on government outside the cabinet departments. For example, the Department of Labor is hardly more than a statistical bureau, the War Labor Board settling most of the problems that would normally be handled in that department. The Department of the Treasury is largely an accounting department. The Reconstruction Finance Corporation and all the various lending agencies are grouped outside the Treasury Department. Many agencies are grouped in the Federal Security Agency, again an agency outside the cabinet.

It might be better if there were a commission to supervise the question of health in the United States, but one thing is certain: it is ridiculous that one must deal with a dozen different departments to find all the agencies connected with health. For

example, the United States Public Health Service used to be in the Treasury Department but is now in the Federal Security Agency. The Child Welfare Department is in the Department of Labor. The Food and Drugs Administration used to be in the Department of Agriculture but is now in the Federal Security Agency. The Immigration Service is in the Department of Interior. The Veterans Administration is entirely independent.

One of the plans that have been suggested for solving the problem of medical care is compulsory health insurance. In the first place, this term is a misnomer. The method has nothing to do with health, it has to do with sickness. It is not insurance, it is a tax. It is in operation in a great many countries in the world, and nowhere has it given as satisfactory records as has the American system based on free enterprise.

Preventable diseases are on the increase, as evidenced in England where the diphtheria rate has gone up since the adoption of compulsory health insurance in 1911 and in Germany, where this rate has tremendously increased. In England, since the adoption of the compulsory sickness insurance act, a higher percentage of patients with far advanced tuberculosis have been admitted to sanatoriums than in the United States.

Compulsory insurance encourages malingering. Days lost by the working man increase instead of decrease. It interposes a third party — the government — between the physician and the patient, the former is responsible to this third party and not to the patient. A poor type of medical care is generated.

In England, a panel system is provided. It is not unusual for a physician to have 1000 or 1500 patients on his panel. He tries to do a little private practice on the side, and it is nothing for him to see thirty patients in the course of an hour. It is easy to see the difficulty of rendering good medical care if the procedure is to allot two minutes to each patient.

There is also a tendency toward mass medicine and this is true throughout the various prominent experiments in compulsory sickness insurance. This was true in Germany before the war, and in this country. During the Depression, the Federal Emergency Relief Administration issued certain edicts to the various states that accepted money from the federal government to carry on medical care, and the physician was told what he could and could not prescribe. He was also told the number of visits that he could make.

The physician is extremely likely to become a certificate writer rather than a family counselor. In fact, a prominent English physician said that under the panel system the physician merely wrote certificates that would satisfy the patient, keep the physician out of the hands of the Medical Council, and satisfy his tattered conscience.

Compulsory health insurance does not in any

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32071

#### PRESENTATION OF CASE

A fifty-four-year-old foreman entered the hospital complaining of substernal pain on exertion.

The patient first consulted his physician four and half years before admission, complaining of anterior chest discomfort of five months' duration. One month before the onset of this symptom, he underwent a herniorrhaphy at another hospital. Physical examination revealed at that time a heart of normal size, but there was a blowing systolic murmur at the apex and a soft blowing diastolic murmur at the base and along the left sternal margin. X-ray films revealed no cardiac enlargement or evidence of aortitis. The electrocardiogram showed a PR interval of 0.3 second. The operation was carried out without difficulty, and convalescence was uneventful. About a month after the operation, he was awakened one night by a vague sensation of uncomfortable pressure across the anterior chest, which lasted half an hour. This sensation recurred about a week later, at which time he found that he was more comfortable sitting up than lying down. This episode also lasted about thirty minutes. A similar but less severe attack awakened him from sleep seven weeks before he saw his physician. He had had no other symptoms.

The past history revealed questionable rheumatic fever sixteen years previous to the onset of symptoms. His heart had been declared normal by an insurance company four years previously. He had had gonorrhea many years ago. He ate heavily and smoked moderately.

Physical examination by his physician revealed a slightly obese man in no distress. The eyes were normal. The maximal apical impulse was felt in the fifth interspace 10 cm to the left of the mid-sternal line. The heart sounds were distant. A moderately loud blowing diastolic murmur was heard in the aortic area and at the apex. There were no thrills. The abdomen was negative. There was no edema of the lower extremities.

The pulse was 78, regular and full. The blood pressure was 140 systolic, 60 diastolic.

A blood Hinton test was negative. A chest plate showed a transverse heart with slight enlargement of the left ventricle. An electrocardiogram revealed normal rhythm, with a rate of 85. The PR interval was 0.28 second,  $T_1$  was inverted,  $T_2$  diphasic,  $Q_1$  slightly prominent, and  $T_4$  inverted.

The patient was advised to lose weight and reduce his smoking. He followed instructions and one month later had lost 14 pounds. During that time he had had no more attacks of chest discomfort and complained only of a little dyspnea.

The patient was again seen by his physician seven months later. He had felt well until a few weeks previously. At that time, he again began to have episodes of substernal discomfort at night, quickly relieved by nitroglycerin. Physical examination was unchanged.

One year later the patient reported that he had been troubled nightly by precordial discomfort, which awakened him but was relieved by nitroglycerin. The pulse was regular at 84. The blood pressure was 135 systolic, 45 diastolic. The heart sounds were fair, with a moderately loud aortic diastolic murmur. There was a questionable diastolic gallop at the apex.

Fifteen months later, he still complained of nightly substernal oppression, which was relieved by nitroglycerin or by sitting up. The pulse was regular at 84. The blood pressure was 150 systolic, 45 diastolic. The heart sounds were of poor quality. Slight systolic and moderate diastolic murmurs were heard in the aortic area. Fluoroscopy revealed no change.

A year later, the patient reported that nightly substernal oppression persisted. The heart sounds were again of poor quality, with Grade II systolic and Grade III diastolic murmurs at the aortic area. Fluoroscopy revealed that the heart was considerably larger than previously. The aorta was rather wide and blunt. The lungs were clear. There was edema of the extremities. At the time of admission to the hospital, four months after last seeing his physician, the patient stated that the substernal oppression had become more frequent and severer, occurring during exertion and at rest. Dyspnea was marked. About a week before admission edema appeared in the ankles and then became generalized. He had been given digitalis and Mercupurin, with little improvement.

The patient was dyspneic. The pupils were equal and reacted to light and accommodation. The heart was markedly enlarged to the left. The sounds were distant. The pulmonic second sound was greater than the aortic. There were slight aortic systolic and diastolic murmurs. The pulse was irregular, with many premature beats. The blood pressure was 120 systolic, 50 diastolic. There were rales in both lung bases. The liver was palpable two finger-

I do not accept the premise that compulsory insurance is necessary, but there are those who say that it is needed for a certain segment of the population. Even if this is so, is that any reason for crowding it down the throats of everyone? Some persons are satisfied with the type of medical care that they have. A national compulsory sickness insurance program would overthrow everything that has produced the best medical education and the best medical care in the world and set up a system that has never been used in this country, and that has certainly never given any outstanding results anywhere else.

This problem can be solved by increasing the efforts on behalf of the voluntary plans, by making them widely available, by increasing diagnostic facilities and by having federal aid where this is necessary to subsidize the various districts.

As I have said before, when the answer is found it will not be a single but a multiple one. Compulsory sickness insurance is not the answer at all. The present system of medical care does need improvement, but this should be accomplished in an evolutionary manner, by increasing the number of facilities for preventive medicine and for diagnosis and making these available at a reasonable cost through hospital insurance, industrial plans, medical-society plans and what not, and by gradually evolving plans — three or four plans of different types — that will cover the whole United States.

In discussing the background of the necessity for reform, let us stick to facts and avoid propaganda. A member of the faculty of this school, in a public address, once stated his belief that organized medicine could not be trusted to handle this problem because, for example, the Medical Society of the State of New York had introduced an amendment to its bylaws that would prevent any individual or county society from initiating any policy that was in conflict with the state society's policies. He did not go on to say that when the amendment came up for consideration in the House of Delegates, it did not receive a single vote. Not even the man who had introduced it voted for it, and when I called that to his attention he said, "Well, the Council approved it." There, again, he displayed his ignorance, because the Council of the Medical Society of the State of New York cannot act on any amendment. If one is introduced, all it can do is to send it to the House of Delegates.

So let us try to make our arguments real arguments and not propaganda. Let us be willing to listen to the other man and sit down with him, and see if we cannot solve the problem in a way that is satisfactory to everyone, and that will not attenuate or deteriorate the present high standards of medical care or medical education, but if possible improve them.

Let us stick to the platform that good medical care should be available for every person in the United States. How many people are without it is not important, because if there is one person in the whole United States who does not receive it, that person is one too many. Let us find a system of distribution of medical care that is in accord with the system of free enterprise, which has made this country what it is.

\* \* \*

In summary, the American Medical Association advocates the following: continued expansion of the practice of medicine, with full development of improved voluntary hospital, medical, indemnity, industrial and commercial insurance against the costs of medical care, the development of public-health and diagnostic facilities for preventive medicine throughout and of adequate diagnostic facilities everywhere, the use of the voluntary insurance principle in caring for the indigent and medically indigent, the development of hospital facilities where present facilities are used to the utmost and are still inadequate (there is now a bill in Congress that we hope will pass, — the Hill-Burton Bill, — which provides for building hospitals in areas lacking them and establishing diagnostic facilities, the bill is not perfect, but it is a step in the right direction), the use of federal funds to aid communities in public-health measures, care of the indigent and construction of necessary hospitals, when these communities are unable to finance the projects, but with retention of local administration, and the creation of a unified United States Department of Health, whether it be a cabinet or a commission.

Finally, let us move ahead, steadily but carefully, in a sound, evolutionary manner. We must not be stampeded into discarding and destroying what has given an unparalleled health record. Let us not forget that private enterprise has made America what it is.

copy without actual infarction in the usual sense of myocardial infarction on a basis of ordinary coronary-heart disease is another possibility. So as the symptom of coronary insufficiency — substernal discomfort — is concerned, there are several points of interest. One is that this symptom began over a year before his hospital admission, after the herniorrhaphy, was fairly acute, occurred when he was in bed at night and then subsided. That is more or less characteristic of a good many cases of coronary insufficiency, especially if the onset is sudden and is preceded by coronary thrombosis. Of course, most of you know that the old concept of coronary insufficiency as a relentless ever-increasing process no longer holds. Dr. White and others\* have shown that many cases undergo considerable improvement in their clinical status coincident with the development of a collateral coronary circulation. When such patients develop so-called "status anginosus," as this man did, they then go on having the symptoms of coronary insufficiency for days or weeks or they die during the episode of acute coronary insufficiency. I do not recall seeing a case in which so pronounced a state of coronary insufficiency existed for so long. This patient reported nightly substernal discomfort for at least two and possibly three years.

When one is presented with a history of this kind the first thing that comes to mind is the possibility of some complication to explain the unusual history. It is conceivable, although not usual, that syphilitic aortitis might produce progressive occlusion of both coronary mouths. In ordinary coronary-artery disease, probably the most important factor in improvement is the development of collateral circulation following occlusion of one of the major branches. If this process were syphilitic, involvement of both arteries at their mouths, in fairly static circumstances, might preclude collateral circulation and yet be compatible with life. Another thing that may contribute to coronary insufficiency is aortic regurgitation, with low diastolic pressure. This sometimes accounts for coronary insufficiency in patients with rheumatic heart disease. Most of the coronary flow takes place during diastole. Therefore, if the diastolic pressure is low, the coronary circulation may suffer accordingly. It is conceivable that the low diastolic pressure here might have been responsible in part for the high state of insufficiency of the coronary circulation.

What are the conditions outside the heart that may be responsible for an increase in the symptoms of pre-existing angina pectoris? It is well known that peptic ulcer, although not necessarily giving rise to symptoms, may prolong coronary symptoms or cause them to be felt in other than usual circumstances. The middle of the night is a good time for

this to occur. Another frequent complication is gall-bladder disease, but there is nothing here to suggest it. The symptoms of hiatus hernia are frequently present at night when the patient is reclining. Such a finding is not mentioned in the x-ray report, but the patient was too sick toward the end to have further investigation. Could he have had pain of this kind as a result of an unusual aneurysm that did not show up in the x-ray films? I doubt it. That diagnosis can be eliminated because of the nature of the pain and especially because of its long duration.

What about dissecting aneurysm? Syphilitic aortitis, if present, is supposed to be a fairly good insurance against dissecting aneurysm, presumably because of its cohesive effect on the layers of the aorta. A number of cases of dissecting aneurysm have been reported, however, in the presence of syphilitic aortitis. It is a rare possibility and need not be considered here.

I shall vote for syphilitic aortitis, with aortic regurgitation, cardiac enlargement, occlusion of the mouths of the coronary arteries, congestive failure, coronary insufficiency and, finally, death with an Adams-Stokes seizure. The question of myocardial infarction of the usual sort must be raised in addition.

#### CLINICAL DIAGNOSIS

Coronary heart disease

#### DR. WILLIAMS'S DIAGNOSES

Syphilitic aortitis  
Aortic regurgitation  
Cardiac enlargement  
Congestive failure  
Occlusion of mouths of coronary arteries, with localized muscle atrophy and fibrosis  
Coronary insufficiency (angina pectoris) (Adams-Stokes syndrome)  
Atherosclerosis of coronary arteries, with old myocardial infarction?

#### ANATOMICAL DIAGNOSES

Syphilitic valvulitis of aortic valve with insufficiency  
Coronary sclerosis with thrombosis  
Chronic passive congestion  
Pleural effusion, bilateral

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: This patient showed a grossly hypertrophied heart, weighing 750 gm. There was a bilateral pleural effusion, which, I believe, can be attributed to passive congestion. The heart showed an abnormality of the aortic valve, characterized particularly by separation of the commissures. The cusps were thickened and shortened, and their points of attachment to the aortic ring were considerably below where they should be. There was

\*White, P. D., Bland, E. F., and Miskall, E. W. Prognosis of angina pectoris: long time follow-up of 497 cases including note on 75 additional cases of angina pectoris decubitus. *J. A. M. A.* 123: 801-804, 1945.

breadths below the right costal margin but was not tender. The ankles showed slight pitting edema.

The white-cell count was 13,000. The hemoglobin was 14.5 gm. The nonprotein nitrogen was 34 mg per 100 cc. The spinal fluid was negative. An x-ray film of the chest showed considerable enlargement of the heart, particularly in the region of the left ventricle. There was some flattening of the apex, and the pulsations were somewhat diminished in this area. The aorta was tortuous but not definitely dilated. There was no calcification of the ascending portion. There was considerable enlargement of the pulmonary vascular shadow, with a tendency to a ground-glass appearance in the medial portions of the lung fields. There was a small amount of fluid in each pleural cavity.

An electrocardiogram showed a high-grade heart block, with frequent dropped beats. The PR interval varied from 0.35 to 0.44 second before the dropped beat.  $T_1$ ,  $T_2$  and  $T_3$  were inverted, R was upright in  $CF_2$ , T was low in  $CF_4$ , and T was inverted in  $CF_6$ . A blood Hinton test was negative.

The day before death the patient began to have generalized convulsions associated with a slow pulse. Twenty-four hours after the onset of these convulsions he complained of severe substernal pain and had another convulsion. A few minutes later he expired, on the eleventh hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR CONGER WILLIAMS: There is a discrepancy in the record in that an abnormal heart was found at the time of operation, whereas nothing was found in an insurance examination a few months later. I shall discard the insurance company's findings.

May we see the x-ray films?

DR MILFORD D. SCHULZ: Only the films taken at the time of his admission to the hospital are available. The striking thing is the enlargement of the hilar and pulmonary vessels, and the diffuse haziness centrally placed in the lung fields. There is no fluid in the pleural sinuses.

DR WILLIAMS: Is this picture sometimes seen on the basis of nephritis alone?

DR SCHULZ: I do not believe that it means that, it is caused by pulmonary edema from any source. You can see it in nephritis and also in cardiac disease.

DR WILLIAMS: Presumably this man died with an Adams-Stokes syndrome, at least the slow pulse and convulsions suggest it.

This middle-aged man presented many significant features in the clinical course of his disease. Aortic valvular disease, with predominant regurgitation, was present for at least seven years. He had cardiac enlargement, which progressed to congestive failure, probably due for the most part to aortic regurgitation. He also had symptoms suggesting coronary insufficiency, which despite great severity persisted for the unusually long period of eight or nine years.

So far as the aortic valve disease is concerned, it was either syphilitic or rheumatic, and other possibilities, such as hypertension and erosion of cusps from infection, can be discarded. If it was syphilitic, the whole picture can be explained on the basis of one disease, which is a popular thing to do at these exercises. The record states twice that the blood Hinton test was negative, and that the spinal fluid was also negative. No mention of the blood Wassermann reaction was made, however, which means that the serologic investigation was incomplete. The highly sensitive Hinton test occasionally shows a prezone that occurs infrequently with the less sensitive Wassermann reaction. I can recall three cases in which the Wassermann test was positive but in which the Hinton test was negative until done in dilutions.

DR TRACY B. MALLORY: That is most unusual, however. Nine times out of ten it works the other way.

DR WILLIAMS: So far as this case is concerned I am not willing to discard syphilis because of the negative Hinton tests. I should be more inclined to do so if blood Wassermann tests were known to be negative, but even that finding does not rule out syphilis.

If we assume that this man had syphilitic aortitis, the symptoms and findings of coronary insufficiency could be explained by the resultant narrowing of the orifices of the coronary arteries, although there is no reason why he should not have had coronary artery disease in addition. At least it would be reasonable to suspect the presence of a syphilitic lesion involving the coronary mouths. X-ray studies might be helpful in that connection. Fluoroscopy reported flattening and localized diminution of pulsations at the apex. One often sees that in myocardial infarction, which of course produces localized muscle weakening, and it does occur with a large area of muscle atrophy and fibrosis following gradual occlusion of the coronary arteries by a syphilitic process.

If he had had rheumatic valvular disease to explain the regurgitation, it is perfectly reasonable to assume that he also had coronary-artery disease. The two are not infrequently associated. It is less easy to explain the prolonged PR interval on the basis of rheumatic infection, because such prolongation usually means an active process. Occasionally, however, prolongation may be permanent after a single attack of rheumatic fever. I should not suppose that this man had had active rheumatic fever over a period of eight or nine years.

So far as the cardiac findings are concerned, the aortic regurgitation alone accounts for most of them. With syphilitic occlusion of the mouths of the coronary arteries, an area of muscle might be sufficiently fibrotic or atrophic to account for localized diminution of the ventricular pulsations by fluor

ds were normal except for enlargement of the nd spots, which remained unchanged Visual acuity on the thirty-sixth day was 20/40 on the ht, and 20/50 on the left (there were no reports the fundi at that time) The craniotomies bulged, d the spinal-fluid pressure remained elevated 50 mm) A combined ventriculoencephalogram i the forty-eighth hospital day was not satisfactory it seemed to be negative The following day the ntient was up and about and was discharged home

When seen in the Out Patient Department one eek after discharge there had been no headache usual acuity was 20/30 on the right, and 20/40 a the left There was papilledema bilaterally — ight on the right and 3 to 4 diopters, with a fresh emorrhage, on the left

*Fourth admission* (eighteen days later) One and half hours before admission the patient had a convulsive seizure, which began in his right hand, progressed up the arm and then became generalized with loss of consciousness The eyes were deviated o the right The seizure lasted five minutes, and he patient felt well and appeared to be normal on admission He was discharged on the following day, 0.1 gm of Dilantin three times a day and 0.1 gm of phenobarbital at night being prescribed

*Fifth admission* (three months later) During his visits to the Out Patient Department, the choking of the left disk decreased but the headaches and frequent severe convulsions persisted The patient was confused and mentally sluggish The right optic disk was somewhat pale, but there was no definite papilledema on either side The subtemporal decompressions were bulging During his stay of three days in the hospital he had one convulsion The Dilantin and phenobarbital were continued

*Final admission* (two and a half months later) The patient took his medicine faithfully and remained well until two weeks before readmission, when he had another convulsion Shortly after this seizure, he became stuporous and was taken to a hospital, where he was given injections "for convulsions" Four days before entry he became comatose, and two days later he began to have convulsions almost continuously On admission he was comatose, breathing heavily The decompressions were bulging and tense The pupils were constricted and did not react to light The eyes wandered continually The tendon reflexes were hypoactive and equal, the plantar reflexes were normal

The temperature was 104°F, the pulse 130, and the respirations 30 The blood pressure was 96 systolic, 50 diastolic

Lumbar puncture yielded clear, colorless fluid under an initial pressure equivalent to 210 mm of water The total protein was 28 mg per 100 cc

A chest plate showed no abnormalities

There were frequent convulsive movements which were severer on the right than on the left

Sodium luminal (0.13 gm subcutaneously) was given at intervals of one or two hours for six doses and after that every three to four hours, the total dosage being 1.43 gm At a second lumbar puncture, the pressure was 190 mm and the fluid was clear and colorless The pulse, which remained rapid, diminished in strength and became irregular, respirations became gasping, the temperature rose to 108.5°, and the patient died thirty-two hours after admission

#### DIFFERENTIAL DIAGNOSIS

DR WILLIAM H SWEET We are not told whether the first part of the seizure was observed, but I presume that the report indicates the full amount of useful clinical data ascertained

"He often bit his tongue, usually on the right side" This comment is the first suggestion of a lateralizing character in the description of the seizures If he bit his tongue more frequently on the right than on the left, presumably the muscles on the left side were more active than those on the right These muscles would be innervated from the right cerebral hemisphere

I should like to see the x-ray films, because they often have crucial diagnostic significance in a case of this kind

DR CLAYTON H HALE These first plain films were reported as negative I do not see anything abnormal The ventriculogram shows that almost all the ventricles are filled and that they are not displaced I cannot be sure, however, that both anterior horns are completely filled The third ventricle is normal The fourth shows no defects

DR SWEET How about this shadow? Is it the anterior horn that did not fill well for some reason?

DR HALE I believe so

DR SWEET It is materially behind one of the others

DR HALE Yes, and the same is true in this film This is one anterior horn, the other apparently stops at this point At least there is overlapping of the two ventricles

DR CHARLES S KUBIK Can you tell which it is?

DR HALE I cannot be sure This one looks smaller and should be the right one, because that was closer to the film The posterior horns look all right The bodies also look normal

DR SWEET The anterior horn stands out much better on the left side than on the right That, of course does not fit in with the one clearly described seizure that has the most localizing significance, namely, the one in which the patient was described as having a seizure that began in the right hand and extended up the arm

In considering the lesions that produce increased intracranial pressure without producing any demonstrable deformity of the ventricular system we are faced with a number of possibilities about which we know little As far back as the turn of the cen-

a separation of 3 to 4 mm between their points of attachment, whereas normal cusps should meet on the aortic wall within 1 mm of each other. So far as I know that is an absolutely pathognomonic sign of syphilitic infection. The aorta immediately above the valve was quite smooth and beyond the arch it showed only ordinary atheroma. There was nothing that I could recognize grossly as being typical of syphilitic aortitis. A section, however, taken just above the commissure, showed focal degeneration of the media of the aorta. Both muscle fibers and elastic tissues were completely destroyed. There was not, however, any inflammatory infiltration, and the vasa vasorum did not show perivascular cuffing, which is usually seen in active syphilitic aortitis.

I believe that the findings justify a flat-footed diagnosis of syphilitic infection but that it was a completely burned-out inactive lesion, which no doubt is the reason for the negative serologic tests. As Dr. Williams has pointed out, it is characteristic in syphilis of the aortic valve to find the mouths of the coronary arteries narrowed by the process. That was not true in this case. Further down in the coronary system, however, in the descending and circumflex branches of the left coronary artery, were old organized thrombi, one of which was slightly recanalized and had again thrombosed. The thrombosis had resulted from atheromatous lesions and had nothing to do with the syphilis, which produced the aortic regurgitation. The myocardium showed irregular patchy fibrosis on microscopical examination but no gross areas of infarction.

## CASE 32072

### PRESENTATION OF CASE

*First admission* A twenty-four-year-old man was admitted to the Emergency Ward shortly after he had had a convulsive seizure.

He stated that he had had a similar seizure several years previously. At the time of admission he was lucid and oriented. The anterior portion of the tongue was lacerated. The pupils were round and equal and reacted to light and accommodation, and the fundi were normal. Neurologic examination was negative.

The temperature was 98°F, the pulse 90, and the respirations 20. The blood pressure was 136 systolic, 84 diastolic.

While in the Emergency Ward, the patient had another convulsion, which lasted about a minute and in which he bit his tongue and was incontinent of urine. Following the convulsion he remained unconscious for about five minutes, after which his mind was again perfectly clear. An electro-encephalogram showed variable waves, with individual frequencies and voltages within normal limits. An

x-ray film of the skull was negative. He was discharged the following day, being advised to take 0.1 gm of Dilantin twice a day and 0.1 gm of phenobarbital three times a day.

*Second admission* (five months later) The patient was admitted in semicoma after several convulsions. Following discharge he had been symptom free until three months later, when he had one seizure. Eleven days before readmission he had two more seizures, and two days before admission he began to have seizures almost continuously. On entry he could be aroused only with difficulty. The tongue was scarred and showed recent lacerations. Examination was otherwise negative.

The temperature was 98.6°F, the pulse 100, and the respirations 20. The blood pressure was 120 systolic, 80 diastolic.

The patient was given 0.13 gm of sodium luminal intramuscularly and had no convulsions during his stay in the Emergency Ward. He was discharged three days after admission, being advised to take 0.1 gm of Dilantin and 0.03 gm of phenobarbital four times a day.

*Third admission* (two weeks later) Soon after discharge the patient began to have constant, severe, throbbing headache in the frontal region and around the eyes. He vomited and was slightly drowsy and said that he had an occasional convulsive seizure. The convulsions usually started with movements of the eyes and then of the body and extremities. He would then fall down, usually on his right side, losing consciousness for one or two hours. He often bit his tongue, usually on the right side, and was incontinent.

Examination showed a papilledema measuring 2 diopters bilaterally and small hemorrhages at the edge of the left optic disk. There was slight peripheral constriction of the visual field of the left eye, and enlargement of the blind spots on both sides. The pupils were regular and equal and reacted to light and accommodation. The neck was slightly stiff. The reflexes were normal, and neurologic examination was negative.

An electroencephalogram showed a large amount of symmetrically distributed, low-voltage, slow activity, with no evidence of focal dysrhythmia. A ventriculogram showed the ventricles to be normal in size, shape and position. Lumbar puncture on the day following the ventriculogram revealed clear fluid under pressure equivalent to 650 mm of water. The total protein was 28 mg per 100 cc. Another ventriculogram, made through anterior burr holes was negative.

The question of a so-called "pseudotumor cerebri" was raised, and subtemporal decompressions were performed, the one on the left being done on the fourteenth hospital day, and the one on the right on the twenty-seventh. On the nineteenth and thirty-sixth hospital days the peripheral visual

ds were normal except for enlargement of the fundi and spots, which remained unchanged. Visual acuity on the thirty-sixth day was 20/40 on the right, and 20/50 on the left (there were no reports of the fundi at that time). The craniotomies bulged, and the spinal-fluid pressure remained elevated (50 mm). A combined ventriculoencephalogram on the forty-eighth hospital day was not satisfactory; it seemed to be negative. The following day the patient was up and about and was discharged home. When seen in the Out Patient Department one week after discharge there had been no headache. Visual acuity was 20/30 on the right, and 20/40 on the left. There was papilledema bilaterally — 1+ on the right and 3 to 4 diopters, with a fresh hemorrhage, on the left.

*Fourth admission* (eighteen days later). One and a half hours before admission the patient had a convulsive seizure, which began in his right hand, progressed up the arm and then became generalized, with loss of consciousness. The eyes were deviated to the right. The seizure lasted five minutes, and the patient felt well and appeared to be normal on admission. He was discharged on the following day, on 1 gm of Dilantin three times a day and 0.1 gm of phenobarbital at night being prescribed.

*Fifth admission* (three months later). During his visits to the Out Patient Department, the choking of the left disk decreased but the headaches and frequent severe convulsions persisted. The patient was confused and mentally sluggish. The right optic disk was somewhat pale, but there was no definite papilledema on either side. The subtemporal decompressions were bulging. During his stay of three days in the hospital he had one convulsion. The Dilantin and phenobarbital were continued.

*Final admission* (two and a half months later). The patient took his medicine faithfully and remained well until two weeks before readmission, when he had another convulsion. Shortly after this seizure, he became stuporous and was taken to a hospital, where he was given injections "for convulsions." Four days before entry he became comatose, and two days later he began to have convulsions almost continuously. On admission he was comatose, breathing heavily. The decompressions were bulging and tense. The pupils were constricted and did not react to light. The eyes wandered continually. The tendon reflexes were hypoactive and equal, the plantar reflexes were normal.

The temperature was 104°F, the pulse 130, and the respirations 30. The blood pressure was 96 systolic, 50 diastolic.

Lumbar puncture yielded clear, colorless fluid under an initial pressure equivalent to 210 mm of water. The total protein was 28 mg per 100 cc.

A chest plate showed no abnormalities.

There were frequent convulsive movements, which were severer on the right than on the left.

Sodium luminal (0.13 gm subcutaneously) was given at intervals of one or two hours for six doses and after that every three to four hours, the total dosage being 1.43 gm. At a second lumbar puncture, the pressure was 190 mm and the fluid was clear and colorless. The pulse, which remained rapid, diminished in strength and became irregular, respirations became gasping, the temperature rose to 108.5°, and the patient died thirty-two hours after admission.

#### DIFFERENTIAL DIAGNOSIS

DR WILLIAM H. SWEET: We are not told whether the first part of the seizure was observed, but I presume that the report indicates the full amount of useful clinical data ascertained.

"He often bit his tongue, usually on the right side." This comment is the first suggestion of a lateralizing character in the description of the seizures. If he bit his tongue more frequently on the right than on the left, presumably the muscles on the left side were more active than those on the right. These muscles would be innervated from the right cerebral hemisphere.

I should like to see the x-ray films, because they often have crucial diagnostic significance in a case of this kind.

DR CLAYTON H. HALE: These first plain films were reported as negative. I do not see anything abnormal. The ventriculogram shows that almost all the ventricles are filled and that they are not displaced. I cannot be sure, however, that both anterior horns are completely filled. The third ventricle is normal. The fourth shows no defects.

DR SWEET: How about this shadow? Is it the anterior horn that did not fill well for some reason?

DR HALE: I believe so.

DR SWEET: It is materially behind one of the others.

DR HALE: Yes, and the same is true in this film. This is one anterior horn, the other apparently stops at this point. At least there is overlapping of the two ventricles.

DR CHARLES S. KUBIK: Can you tell which it is?

DR HALE: I cannot be sure. This one looks smaller and should be the right one, because that was closer to the film. The posterior horns look all right. The bodies also look normal.

DR SWEET: The anterior horn stands out much better on the left side than on the right. That, of course, does not fit in with the one clearly described seizure that has the most localizing significance, namely, the one in which the patient was described as having a seizure that began in the right hand and extended up the arm.

In considering the lesions that produce increased intracranial pressure without producing any demonstrable deformity of the ventricular system, we are faced with a number of possibilities about which we know little. As far back as the turn of the cen-



a separation of 3 to 4 mm between their points of attachment, whereas normal cusps should meet on the aortic wall within 1 mm of each other. So far as I know that is an absolutely pathognomonic sign of syphilitic infection. The aorta immediately above the valve was quite smooth and beyond the arch it showed only ordinary atheroma. There was nothing that I could recognize grossly as being typical of syphilitic aortitis. A section, however, taken just above the commissure, showed focal degeneration of the media of the aorta. Both muscle fibers and elastic tissues were completely destroyed. There was not, however, any inflammatory infiltration, and the vasa vasorum did not show perivascular cuffing, which is usually seen in active syphilitic aortitis.

I believe that the findings justify a flat-footed diagnosis of syphilitic infection but that it was a completely burned-out inactive lesion, which no doubt is the reason for the negative serologic tests. As Dr. Williams has pointed out, it is characteristic in syphilis of the aortic valve to find the mouths of the coronary arteries narrowed by the process. That was not true in this case. Further down in the coronary system, however, in the descending and circumflex branches of the left coronary artery, were old organized thrombi, one of which was slightly recanalized and had again thrombosed. The thrombosis had resulted from atheromatous lesions and had nothing to do with the syphilis, which produced the aortic regurgitation. The myocardium showed irregular patchy fibrosis on microscopical examination but no gross areas of infarction.

## CASE 32072

### PRESENTATION OF CASE

*First admission* A twenty-four-year-old man was admitted to the Emergency Ward shortly after he had had a convulsive seizure.

He stated that he had had a similar seizure several years previously. At the time of admission he was lucid and oriented. The anterior portion of the tongue was lacerated. The pupils were round and equal and reacted to light and accommodation, and the fundi were normal. Neurologic examination was negative.

The temperature was 98°F, the pulse 90, and the respirations 20. The blood pressure was 136 systolic, 84 diastolic.

While in the Emergency Ward, the patient had another convulsion, which lasted about a minute and in which he bit his tongue and was incontinent of urine. Following the convulsion he remained unconscious for about five minutes, after which his mind was again perfectly clear. An electroencephalogram showed variable waves, with individual frequencies and voltages within normal limits. An

x-ray film of the skull was negative. He was discharged the following day, being advised to take 0.1 gm of Dilantin twice a day and 0.1 gm of phenobarbital three times a day.

*Second admission* (five months later) The patient was admitted in semicomatose after several convulsions. Following discharge he had been symptom-free until three months later, when he had one seizure. Eleven days before readmission he had two more seizures, and two days before admission he began to have seizures almost continuously. On entry he could be aroused only with difficulty. The tongue was scarred and showed recent lacerations. Examination was otherwise negative.

The temperature was 98.6°F, the pulse 100, and the respirations 20. The blood pressure was 125 systolic, 80 diastolic.

The patient was given 0.13 gm of sodium luminal intramuscularly and had no convulsions during his stay in the Emergency Ward. He was discharged three days after admission, being advised to take 0.1 gm of Dilantin and 0.03 gm of phenobarbital four times a day.

*Third admission* (two weeks later) Soon after discharge the patient began to have constant, severe, throbbing headache in the frontal region and around the eyes. He vomited and was slightly drowsy and said that he had an occasional convulsive seizure. The convulsions usually started with movements of the eyes and then of the body and extremities. He would then fall down, usually on his right side, losing consciousness for one or two hours. He often bit his tongue, usually on the right side, and was incontinent.

Examination showed a papilledema measuring 2 diopters bilaterally and small hemorrhages at the edge of the left optic disk. There was slight peripheral constriction of the visual field of the left eye and enlargement of the blind spots on both sides. The pupils were regular and equal and reacted to light and accommodation. The neck was slightly stiff. The reflexes were normal, and neurologic examination was negative.

An electroencephalogram showed a large amount of symmetrically distributed, low-voltage, slow activity, with no evidence of focal dysrhythmia. A ventriculogram showed the ventricles to be normal in size, shape and position. Lumbar puncture on the day following the ventriculogram revealed clear fluid under pressure equivalent to 650 mm of water. The total protein was 28 mg per 100 cc. Another ventriculogram, made through anterior burr hole, was negative.

The question of a so-called "pseudotumor cerebri" was raised, and subtemporal decompressions were performed, the one on the left being done on the fourteenth hospital day, and the one on the right on the twenty-seventh. On the nineteenth and thirty-sixth hospital days the peripheral visual

is obvious that, to retain our faith in some sort of desirable destiny for mankind, we must look on our disintegrated present to the inevitable interaction when we will again right ourselves, realize the inescapable responsibilities of existence, face the barriers between ourselves and a newer, higher goal. There is nothing in our past experience to deny such a belief, there is everything to confirm it. We are again merely witnessing the devious ways by which man works toward each successive improvement.

### SENSING OF OSTEOPATHIC PHYSICIANS IN MASSACHUSETTS

For the last thirty-seven years certain graduates of osteopathic schools have been permitted to practice osteopathy or medicine in Massachusetts. In view of recent changes in the statutes, it seems desirable to review the acts of the General Court that have governed such practice. In 1909 the Legislature enacted a law that contains the following statement, "The terms osteopathy and osteopathic, as used in this act or in relation to the registration and practice of osteopathic physi-

cians, shall have the same legal construction and meaning as the terms medicine and medical." Another section of this act states that persons registered under the act shall not be permitted to prescribe or administer drugs for internal use, or to perform major operations in surgery, or to engage in the practice of obstetrics, or to hold themselves out by virtue of such registration as and for other than osteopaths. The latter section applied to certain men who had been graduated from an osteopathic college, who had been practicing in Massachusetts for four years previous to the passage of

the act and who wished to be registered as osteopaths and limit their practice to osteopathy. Some doctors took advantage of this law and continued to practice nothing but osteopathy, but probably few of them remain.

From 1909 until the middle of 1944 graduates of any medical school, osteopathic or regular, were eligible to take the examination of the Massachusetts Board of Registration in Medicine, irrespective of the quality of the school from which they had graduated. But in 1936 the so-called "Approving Authority Law" was passed, which stated that students who matriculated at a medical school on or after January 1, 1939, must have graduated from a school approved by the Approving Authority. The effective date was subsequently changed to January 1, 1941. This act also specified

that, for the purposes of the Approving Authority, schools approved by the American Osteopathic Association and schools approved by the American Medical Association would receive the same consideration. It was because of the latter that the Approving Authority never did accept the list of the schools approved by the Council on Medical Education and Hospitals of

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

George L. Schadt, *Chairman*  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

the American Medical Association

At the last session of the Legislature, apparently because they feared that the Approving Authority never would approve osteopathic schools, the osteopaths introduced legislation to set up an osteopathic board of registration, but the bill was withdrawn. Finally, at the suggestion of the Committee on Education of the Legislature, a compromise bill was drawn and finally passed. The bill states that the Approving Authority shall be increased from three to five members, one member being the osteopathic member of the Board of Registration in

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## ACTION AND REACTION

IT SEEMS to be a general law of nature that every action has its reaction, as the discharge of a gun is followed by the recoil. The seasons succeed one another, with winter as the inevitable reaction to summer, the rain and the sun each in turn exercise their influence in stimulating growth, seeming to oppose but actually complementing each other, the reed bows before the wind, then seeks its original position. So, in higher levels of activity, we appear to have compensating forces that can be depended on to oppose right actions and, eventually, to correct wrong ones. Only the wave lengths may vary; the reactions may be incredibly swift or, in the case

of massive forces, we may have to wait long for them to manifest themselves.

At the moment we are in the midst of a postwar reaction that shocks us like a hammer blow—a depression marking the release of those moral forces, as we considered them, that had been confined and directed toward a single, presumably noble and unselfish, purpose. We knew at the time that this reaction would set in, but still we were unprepared for it when the war went out from under us.

That which we had accepted and on which we had depended as unselfish devotion to a noble cause gave way to the return, sometimes manyfold, of selfishness and greed. The issues on which we had taken our stand became confused, the goals that we had seemed to reach became as unreal as the rainbow's end. Each one saw, not a better world for himself and others, but the need for hurrying back into the old warren before someone else could reach it.

We see this precipitate abandonment of the ideals that we had thought we had in hand in the wave of labor difficulties that has swept the country, we see it in the dissatisfaction of our less seasoned veterans who clamor only to get home, and in the disgraceful and subversive activities that have been reported to us of men and officers alike still in foreign countries. We see it in many little ways,—in the petty selfishnesses and discourtesies of the highway, in the increased demands made on our own harassed profession and in the abandonment of those restraints that commitment to a common cause had placed on us,—and we know that our tide of common effort has reached its flood and has begun to run the other way.

It has become popular, too, in our free press, which can roar defiance like a lion when needed to follow now in the footsteps of certain less regal animals. With a crying need for constructive effort in every direction, some of our editors seem more interested in digging up old bones to chew on and in indulging in what seems to us to be vicious anti-Russian propaganda. Our politics also, or our statesmanship, if you will, seems not now to be of the high order that our victories require to make the winning of them both justifiable and reasonably permanent. There is much with which we have a right to be discontented at the present time.

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## TRANSDIAPHRAGMATIC RESECTION OF THE VAGUS NERVES FOR PEPTIC ULCER\*

FRANCIS D MOORE, M D,† WILLIAM P CHAPMAN, M D,‡ MILFORD D SCHULZ, M D,§  
AND CHESTER M JONES, M D ¶

BOSTON

DURING the last fifty years, a variety of surgical maneuvers have been developed for the treatment of cases of peptic ulcer|| that may be broadly termed as intractable to therapy but are otherwise uncomplicated. According to Allen,<sup>1</sup> approximately 10 of every 100 patients suffering from peptic ulcer who present themselves to a physician do poorly under ordinary nonoperative methods of treatment. A sizable fraction of this group develop hemorrhage, perforation or cicatricial obstruction, obviously requiring surgical intervention. The remainder—estimated by Allen and Welch<sup>2</sup> as 10 per cent—stand as medical failures or as intermittently sick patients who, tied down to their diet and medication, still present symptomatic difficulties and an economic status far removed from that of a well man.

In these cases that prove refractory to medical treatment, surgery has in the past been directed at several objectives. One of these has been to increase the patency of the pylorus, another to produce some change in the relation between the acid gastric content and the alkaline duodenal or jejunal content, resulting in a neutralization effect of some type, and a third to ablate acid-forming cells, thus lessening gastric acidity.

That such physiologic objectives have not always been attained is easily demonstrated. Study of many patients after posterior gastroenterostomy reveals bile-free material in the stomach<sup>3</sup> that is of high titratable acidity and low pH. Subtotal resection leaves in place much tissue containing parietal cells<sup>4</sup> and is also compatible with high

postoperative acidity,<sup>5</sup> although fundusctomy<sup>6</sup> has represented an effort to circumvent this physiologic contradiction. Subtotal gastric resection may owe its success largely to removal of the antral mucous membrane rather than to the ablation of parietal cells,<sup>6-8</sup> and there is experimental evidence<sup>9-11</sup> that the antrum occupies an important place, both in the normal secretory mechanism and in the so-called "ulcer mechanism." The occasional patient who remains chronically malnourished and develops peculiar postprandial symptoms following subtotal gastric resection brings to mind the possibility that this operation may be detrimental to the nourishment of some patients.<sup>12</sup>

The operative hazards of subtotal gastrectomy must be considered in evaluating this operation, and although they have been markedly reduced in recent years by doing the operation in stages<sup>7, 13</sup> or by removing the antral mucosa in the presence of an inflamed duodenum,<sup>2, 8, 14</sup> the operation still carries the inherent risks of an anastomotic gastrointestinal procedure. The postoperative incidence of stomal or jejunal ulcer following subtotal gastric resection is variously estimated at 2 to 8 per cent.<sup>15, 16</sup>

It is a familiar observation that patients with peptic ulcer are worse during periods of so-called "stress"<sup>17-19</sup>. Such experiences accumulating over the years have led to the conclusion in the minds of clinicians everywhere that there is a close correlation between events in the cerebral cortex and functional activity in the stomach. The work of Cushing<sup>20</sup> with duodenal ulcer in certain types of brain lesions furnishes corollary information bearing on this problem, and also suggests that changes above the foramen magnum can produce ulceration in the upper gastrointestinal tract.

The manner of connection between the brain and the stomach has been known for many years. The vagus nerves were first studied in relation to gastric physiology by Pavlov,<sup>21</sup> who showed in dogs that following section of both nerves gastric secretion in response to sham feeding and conditioned reflexes was lost. This bit of evidence alone

\*From the Department of Surgery and the Department of Medicine, Harvard Medical School, and the Gastrointestinal Clinic, Massachusetts General Hospital.

This study was supported in part by a grant from the Josiah Macy Jr. Foundation.

†Assistant in surgery, Massachusetts General Hospital, instructor in surgery, Harvard Medical School.

‡Assistant in medicine, Massachusetts General Hospital and Department of Medicine, Harvard Medical School.

§Radiologist, Massachusetts General Hospital.

¶Physician, Massachusetts General Hospital, clinical professor of medicine, Harvard Medical School.

||In this paper the term "peptic ulcer" is used to apply to benign ulcerations of the esophagus, stomach, duodenum or jejunum. It is employed as a generic term for this group of ailments and is not intended to imply that peptic is of special significance in their formation.

Medicine, who shall be a graduate of a school approved by the American Osteopathic Association and by the Approving Authority, and the other a layman

On December 14, 1945, the newly designated Approving Authority took favorable action on two schools approved by the American Osteopathic Association, namely, the Kirksville College of Osteopathy and Surgery, Kirksville, Missouri, and the Philadelphia College of Osteopathy and Surgery, Philadelphia. This approval followed hearings at which representatives of both schools presented all the facts concerning the qualifications demanded by the Approving Authority for medical schools. The Approving Authority had previously denied approval to the Des Moines Still College of Osteopathy, Des Moines, Iowa, which is a school approved by the American Osteopathic Association, an action indicating that the Approving Authority has not been giving blanket approval to all schools approved by the American Osteopathic Association.

As a result of these changes in the law controlling the practice of medicine in the Commonwealth and the actions of the Approving Authority, all applicants for examination for registration who matriculated on or after January 1, 1941, must be graduates of medical schools or osteopathic schools that have been judged worthy of approval. It also means that, in the future, the people of Massachusetts who need medical attention will be given it by either osteopathic or regular physicians who have received a proper education.

## NOTICES

### INTENSIVE COURSE IN OPHTHALMOLOGY

The Ophthalmological Study Council offers an intensive course covering various aspects of ophthalmology and extending from April 1 to June 1. This is primarily intended for discharged medical officers, but any physician who is properly qualified may participate. No laboratory or clinical work will be included, instruction being carried out by lectures, required reading and seminars. The course has been arranged by the executive officers of the Council, — Drs. Walter B. Lancaster, S. Judd Beach, T. L. Terry and Trygve Gundersen and Colonel Phillips Thygeson, — with the help of a large group of prominent ophthalmologists from all parts of the country, and it has the approval of the Surgeons General of the Army and of the United States Public Health Service.

Further details are given on the advertising pages of this issue of the *Journal*. Additional information may be obtained from the Ophthalmological Study Council, 520 Commonwealth Avenue, Boston 15.

### BOSTON UNIVERSITY COURSE FOR DISCHARGED MEDICAL OFFICERS

Boston University School of Medicine will offer a months' course for medical officers who have been discharged from the armed forces. This course has been designed to provide opportunity for these men to acquaint themselves with recent advances in medicine, to prepare themselves for practice or to spend a short period advantageously while waiting for a hospital appointment. Teaching by the case method will be conducted on the wards and in the outpatient departments of the hospitals affiliated with the medical school. In addition, regular teaching exercises will be held sometimes a week. Special conferences or seminars will be arranged as occasion arises.

Instruction in the following fields will be offered: internal medicine, general surgery, orthopedic surgery, obstetrics and gynecology, urology, otolaryngology and radiology. If there is a demand for instruction in the preclinical sciences, courses in these subjects may be arranged. The student is urged to spend the entire six months in one of the above fields, but arrangements can probably be made to permit a few students to divide their time between two or more of the fields listed above if they so desire.

The course will begin on March 15 and will extend to September 15. The tuition fee will be \$375.00. Application for admission should be made by writing to the Office of the Dean, Boston University School of Medicine, 80 East Concord Street, Boston 18.

### BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held in the Amphitheater of the Peter Bent Brigham Hospital, Boston, on Wednesday, February 20, at 8 p.m.

#### PROGRAM

The Comparative Pathologic Physiology of Addison's Disease and Cushing's Syndrome. Dr. Edwin Kepler.  
Studies on the Stress Response of the Adrenal Cortex in Man. The diurnal rhythm. Dr. Gregory Pincus.  
Studies on the Stress Response of the Adrenal Cortex in Man. Anoxia and shock therapy. Dr. Hui Hoagland.

### SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, February 19, at twelve noon. Dr. Harlan F. Newton will speak on the subject "Surgery in Pulmonary Tuberculosis." Physicians are cordially invited to attend.

### MASSACHUSETTS HOSPITAL ASSOCIATION

The Massachusetts Hospital Association will hold its annual meeting for the election of officers and such other business as may arise at the Hotel Statler on Monday, March 11, at twelve noon. This is to be a luncheon meeting.

### NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held on Thursday, February 21, at 8 p.m., in the amphitheater of the Peter Bent Brigham Hospital, Boston. The program is as follows:

Case Reports  
Liposarcoma. Drs. Austin L. Vickery and R. Cataldo.  
Fibrosarcoma of the Heart Valve. Drs. Ephraim and Austin L. Vickery.  
Homologous Serum Jaundice. A problem in the operation of a blood bank. Drs. I. Herbert Schein, Charles A. Janeway and Thomas D. Kinney, with assistance of Virginia S. Poole and Ianthé Taylor.  
Skeletal Growth in Relation to Vitamin A Deficiency and Excess. Dr. S. B. Wolbach.

Short business meeting

(Notices continued on page viii)

the Mann-Williamson anastomoses. One group consisted of 3 otherwise normal dogs, another composed 3 dogs with the sympathetic nerves cut, and third consisted of 3 dogs with the parasympathetic supply to the stomach cut. The only animals that did not develop peptic ulcers were those in which the vagus nerves had been cut.

In 1922 Latarjet<sup>21</sup> and in 1932 Pieri<sup>22,23</sup> worked the vagus section in human beings, using the transdominal route. Their results are difficult to evaluate, but it is important to observe that, although some relief was secured, the effect was apparently extremely short-lasting.

In 1926, McCrea<sup>24</sup> published a review covering the nerve supply to the stomach and its significance and discussed part of the physiologic mechanism involved. He pointed out that vagal section in the chest produces marked motor effects on the stomach. Most of these effects have been corroborated by our work in human beings.

During the last five years, following the work of Churchill and Sweet,<sup>35</sup> a large number of trans-thoracic gastrectomies have been performed in many centers in this country, the aggregate total of which must run to several hundred. Observations on patients of this type in whom both vagus nerves were sectioned at variable distances above the diaphragm have shown that although disorders of pyloric emptying may develop, those of pancreatic or hepatic function or absorptive ability of the upper small bowel do not. This indicates that vagus section at this level is not deleterious to the upper digestive mechanism.

Another recent surgical development of significance is the work of Smithwick<sup>36</sup> dealing with surgery on the other component of the autonomic system. Several fundamental considerations that are applicable to the vagus nerves have emerged from his work. The first relates to what one might call thoroughness of operation. Smithwick has shown that a lasting result can best be obtained by radical extirpation of the autonomic system involved. This fact, among others, has led us to perform a vagus resection in which the nerve is resected from just below the lung root to well down on the stomach wall. Smithwick has also shown that the autonomic nervous system regenerates rapidly, particularly through tissue planes and ordinary ligatures. This has led us to believe that ideally the diaphragm should be cut and interposed between the cut ends of the nerves.

With these considerations in the background, work in this field was begun at the Massachusetts General Hospital early in 1944, and to date 15 patients have been operated on.

For some time prior to 1944, Dragstedt and his co-workers<sup>37</sup> had been working with a similar procedure and had already operated on several patients and published a preliminary account of their results. Since then, Dragstedt<sup>38,39</sup> has published

more of his findings in patients on whom this operation had been carried out. His observations have been most helpful to others working in this field, and to him should go the credit for reviving this apparently obsolete operation.

In studying our patients we have directed attention toward the qualitative and quantitative aspects of the secretory changes, as well as to alterations in motility, as recorded by the balloon kymograph, to motility, as gauged by x-ray examinations and to changes in afferent conduction of painful stimuli from the upper gastrointestinal tract. These results will be briefly reported so that the findings may be compared with other work going on at the present time<sup>39,40</sup> and so that a preliminary appraisal of the procedure may be provided.

#### CLINICAL DATA AND RESULTS

A summary of the first 12 cases that were operated on is shown in Table 1. Two patients were women and 10 were men. Four patients had duodenal ulcer without other complications. One had a co-existent esophageal ulcer and Raynaud's disease. Two patients had jejunal ulcers in old gastroenterostomies, and 1 of these had a concomitant duodenal ulcer. Two patients had stomal ulcers following gastric resection. Two patients had gall-bladder disease as well as duodenal ulcer. One had a submaxillary carcinoma, controlled by neck dissection and x-ray treatment, as well as a duodenal ulcer.

These 12 cases represent some of the most difficult therapeutic problems encountered in this field. They were selected because of the long duration and intractability of the symptoms as well as the past and present complications. All the patients had had one or more rigorous terms of hospital medical treatment in an attempt at relief. They were chosen in the hope that good or bad results would soon become apparent and with the idea that a maintained good result was significant and not due to chance factors.

In addition to these 12 patients, 1 patient was operated on at this hospital by another member of the staff as a desperate measure because of repeated massive sublethal gastric hemorrhages. He did not have a duodenal ulcer, nor had he been shown to have peptic ulceration at any time, and he does not fall into this group of cases. The patient succumbed approximately forty-eight hours following the operation, owing to difficulties that were apparently related to the anesthesia but that could also have resulted from hyperirritability of the autonomic nervous system, with the setting up of vagovagal reflexes and resultant cardiac standstill. The case is mentioned because it should be remembered that, as is true of any open chest procedure, this operation carries definite hazards, and following this event which took place early in our experience with this procedure we have routinely

suggests that the vagus nerves constitute one of the main pathways, if not the main one, between the cerebrum and the upper gastrointestinal tract. Other possible pathways include the sympathetic and somatic nerves and circulating humoral factors. The sympathetic side of the autonomic nervous system is doubtless significant in the physiology of the upper gastrointestinal tract, and it is probable that one of its more vital functions is the conduction of afferent impulses,<sup>22</sup> many of which reach the conscious level and may be called viscerosensory fibers as well as regulatory fibers serving motor and secretory end organs.<sup>23</sup> Circulating factors involved in the secretory mechanisms of the stomach have been extensively investigated by many workers, chief among them Ivy<sup>24</sup> and his group at Northwestern University. The relation between the enteric hormones that they are studying and the antral hormones described by Edkins<sup>9</sup> in 1906, which may be involved in the success of ordinary subtotal gastrectomy, is not clear. As a working hypothesis, however, one might suggest that impulses coming down the vagus nerves stimulate end-organ cells in the antrum whose secretion is both internal and external, the external secretion becoming a small fraction of the digestive mixture of the stomach and the internal secretion serving as a local perpetuating mechanism to complete the process of digestion after the initial psychologic stimuli of the sight of food and its chewing and swallowing have ended.<sup>10</sup>

These considerations in patients with peptic ulcer are profound and far-reaching in their significance. Most patients with peptic ulcer are likely to have pain when the stomach is empty. The pain is actually relieved by eating, despite the fact that this produces more acid secretion, as frequently demonstrated in the ordinary gastric analysis. When, however, a gastric analysis is carried out through a twenty-four-hour or forty-eight-hour period, it will be seen that the taking of food, although it may increase the total chloride content and the total amount of gastric secretion, is actually accompanied by a decrease in acidity.<sup>3</sup> One may logically conclude from this that the secretory mechanism that operates on the fasting stomach is the one of the greatest importance in determining the therapy of patients with peptic ulcer. The evidence at hand suggests that neural factors are the important ones in the secretion and reaction of the fasting stomach, whereas the humoral factors play a leading role in the postprandial digestive process.

By this line of reasoning, one is brought to a possible approach to the vagus nerves in the treatment of peptic ulcer. There are many other considerations that form the background for this procedure, but those that have been mentioned above seem to be the most essential ones. Other less vital considerations are as follows. One of the drugs most effective in the treatment of early peptic

ulceration is atropine. This drug apparently acts by altering the permeability of the cell to acetylcholine and thus blocking parasympathetic impulses at the end organ. If the parasympathetic nerve supply to the stomach and duodenum were adequately interrupted, one might reasonably assume that a permanent and complete atropinization of the area had been secured and could conclude that such a procedure might help the patient with peptic ulcer.

Another element of some significance has to do with the concepts that are broadly grouped under the term "psychosomatic medicine." As Cobb<sup>25</sup> has so aptly put it, the use of the term "psychosomatic" predicates a false dichotomy and possibly should be avoided. The fact remains, however, that disturbances in the mental realm may at times be translated into organic disease through the mediation of either neural or humoral pathways. Peptic ulceration probably falls into this group of ailments, and it is possible that decentralization of the stomach through section of the nerve supply would prevent such environmental factors from affecting the organ.

#### SURGICAL BACKGROUND

After the work of Pavlov, interest in vagus effects on the stomach does not figure prominently in the literature, possibly owing to the rise and extensive use of posterior gastroenterostomy as an operative procedure and to the experimental work of Edkins.<sup>9</sup> In 1924, however, Stahnke,<sup>26</sup> in experiments involving chronic electrical stimulation of the vagus nerves, produced typical peptic ulceration in 2 of 5 dogs, a result that, although numerically unimpressive, is of considerable qualitative significance as regards possible mechanisms relating to clinical peptic ulceration.

In 1929, Hartzell<sup>27</sup> using dogs, demonstrated in a convincing manner three fundamental points relative to the vagus nerves. The first is that section of both nerves decreases the acidity of the gastric contents. The second is that this section cannot be adequately done unless it is made through the chest. The third point is that if the section is technically incomplete, the effect is disappointing and transient. Restudy of these dogs three years after the initial operation showed a return of the acidity.<sup>28</sup> This finding, among others, has prompted us to carry out the most complete vagus resection possible in the lower chest and upper abdomen.

In 1931, Beaver and Mann<sup>29</sup> published a short paper that is of the greatest interest in this field. They were working with the Mann-Williamson preparation, which, in their experience, produced ulceration in dogs in approximately 95 to 98 per cent of cases.\* In the article mentioned, they describe three sets of experiments on dogs prepared

\*In the Mann-Williamson<sup>29</sup> preparation unneutralized gastric secretions are poured into the upper jejunum unprotected by the alkaline hepatic and pancreatic juices, which have been sidetracked into the lower bowel.

returning for studies. During these return visits, no recurrence has been observed, with one exception, consisting of a tiny duodenal fleck seen approximately eight months after operation, which again disappeared and was not accompanied by any return of symptoms. Following operation, as a general rule, the patients were allowed to eat and drink anything they wished, including alcohol and coffee, since it was believed that the operation would not be put to an adequate test if a patient was carried along on conscientious medical therapy.

One patient had symptoms over a six-month or eight-month period that were referable to increased gastric emptying time. These symptoms consisted of occasional belching and vomiting of food eaten many hours previously. The vomiting never became serious enough to alter the blood electrolyte con-

centrations and have returned to work. A patient with stomal ulcer following subtotal gastric resection, in which remaining antral tissue was present, was only gradually relieved of his symptoms. He later had the antral remnant removed, with complete healing.

In summary, it may be said that in all 12 cases the ulcers have healed or are healing and that all but 1 patient had immediate and sustained symptomatic relief. There have been no surgical complications, such as empyema, persistent pneumothorax and cardiospasm.

### X-Ray Changes

The x-ray changes following vagus resection may be described as consisting of prolongation of the initial emptying of barium into the duodenum

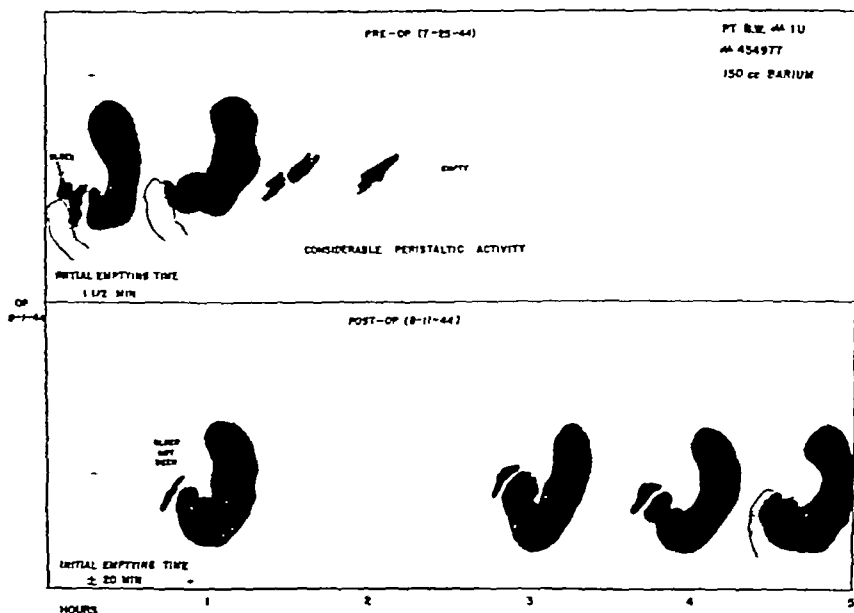


FIGURE 1 Tracings of Serial Spot Films of Stomach and Duodenum in Case 1. These demonstrate the gastric emptying time by x-ray, preoperatively and postoperatively. Some peristaltic activity was still visible postoperatively under the fluoroscope, but it had markedly decreased. There was residual barium in the stomach at fourteen hours.

centration, which remained normal throughout this period, but the patient lost several pounds in weight. This finally ceased, and the patient has since remained well.

Nine patients had duodenal or jejunal ulcers that produced pain as their outstanding symptom. In 2 of these cases, the pain was so severe that the patient was obliged to ingest some sort of antacid preparation frequently throughout the day and night. The clinical result in most of these patients has been quite striking in that they have had immediate and lasting relief of their symptoms. Whereas they were ready to submit to any type of medication or surgery to rid themselves of the symptoms, which plagued them constantly, they have been

and marked prolongation of the final emptying time of barium from the stomach. In normal patients, the initial time of barium-emptying into the duodenum is from half a minute to one and a half minutes after taking barium by mouth. This has not been altered by the presence of peptic ulcer unless the patient has frank obstruction. In the patients who have had vagus resection, initial emptying into the duodenum usually requires fifteen to twenty minutes.

The final emptying time of the normal stomach is approximately two to two and a half hours. Following vagus resection, this time may be twelve to twenty-four hours (Fig 1). It is remarkable that these changes have not produced more symp-



novocainized both vagus nerves above the point of manipulation and have given rather large doses of atropine either before or during the operation

The report of the clinical results in these 12 cases must be regarded as an interim one, because it will

cated duodenal ulcers no crater was visible by x-ray a week to ten days after the operation. In 2 cases, stomal ulcers following gastrojejunostomy required a longer time to heal but finally reached complete healing in three weeks. Follow-ups on

TABLE 1

CASE No	HOSPITAL No	AGE	SEX	DIAGNOSIS	DURATION OF ULCER SYMPTOMS	PREVIOUS COMPLICATIONS	SYMPTOMS	DATE OF OPERATION	RESULT	COMMENTS
1	454977	37	M	Duodenal ulcer	15	Bleeding (1944)	Mild pain	Aug 1, 1944	Symptoms relieved ulcer healed	Possible recurrence, April, 1945, cure restudied, June, 1945 ulcer now healed and patient well.
2	433311	42	F	Duodenal ulcer esophageal ulcer, hiatus hernia Raynaud's disease	5	None	Epigastric pain	Aug 4, 1944	Ulcer healed and pain relieved symptoms from slow emptying bothersome for 6 mo	Esophageal ulcer visible by x-ray April, 1945, dorsal sympathectomy April 1945 cure restudied, Aug 1945, patient now well and without symptoms.
3	270852	52	M	Duodenal ulcer metastatic cancer of submaxillary region	18	Perforation (1927) bleeding (1929 and 1941)	Severe epigastric pain	Dec 26, 1944	Striking symptomatic relief, with rapid healing of ulcer	Case restudied, August, 1945, excellent result maintained, both clinically and by laboratory studies.
4	479283	41	M	Jejunal ulcer duodenal ulcer polycythemia vera	22	Perforation (1932) posterior gastroenterostomy (1932) bleeding (1938) anterior gastroenterostomy (1939)	Severe epigastric pain	Feb 26, 1945	Striking symptomatic relief, with rapid healing of both ulcers	Case restudied, August, 1945 excellent result maintained both clinically and by laboratory studies.
5	480224	61	M	Jejunal ulcer possible paranoia	32	Perforation (1925) posterior gastroenterostomy (1934)	Severe epigastric pain	March 6, 1945	Good symptomatic relief with rapid healing of ulcer	Case restudied, August, 1945 good maintenance of result.
6	488327	54	M	Duodenal ulcer possible psychoneurosis	3	None	Atypical epigastric pain, unrelieved by alkali	June 8, 1945	Ulcer healed one component of pain disappeared	Patient still has some epigastric pain, poorly selected case.
7	169114	40	M	Duodenal ulcer	14	Bleeding (1938 and 1941)	Typical ulcer pain	June 15, 1945	Excellent symptomatic result with rapid healing of ulcer	Case restudied August, 1945 good maintenance of result, no change in gall bladder motility by x-ray
8	37800	43	F	Duodenal ulcer chronic cholecystitis hypertension	16	Bleeding (1939 1942 and 1945)	Epigastric pain	Aug 14, 1945	Pain relieved intermittent vomiting for 1 wk post-operatively ulcer healed	Some delay at cardia shown by x-ray; possible cerebrovascular accident, September 1945
9	381380	35	M	Duodenal ulcer	3	Perforation (1944)	Epigastric pain	Aug 15, 1945	Excellent symptomatic result ulcer healed	
10	231542	50	M	Stomal ulcer cholelithiasis	23	Gastroduodenostomy (1932) bleeding (1934) subtotal gastrectomy (1935) bleeding (1945)	Pain	Aug 28, 1945	Excellent ulcer healed	
11	501746	37	M	Stomal ulcer	18	Subtotal gastrectomy (1944) obstruction and operation (1945)	Severe epigastric pain	Sept 7, 1945	Very gradual improvement ulcer healing	Antral remnant still in place response slow but definite complete healing on removal of antral remnant.
12	502947	31	M	Duodenal ulcer	5	None	Pain and vomiting	Sept. 20, 1945	Good result ulcer healed	Ulcer previously failed to heal after 2 mo of intensive therapy

be many years before this operation can in any way reach final evaluation

As regards healing of the ulcer, in the uncompli-

all these patients have been carefully carried out, and most of the patients have been grateful for their treatment and have been co-operative in

in place, both of which are admittedly artificial stimuli  
The permanence of these secretory changes cannot as yet be determined They have been main-

able to assume that there would be some change in reaction to neostigmine The studies so far have been disappointing, not for lack of postoperative findings but because the neostigmine secretory

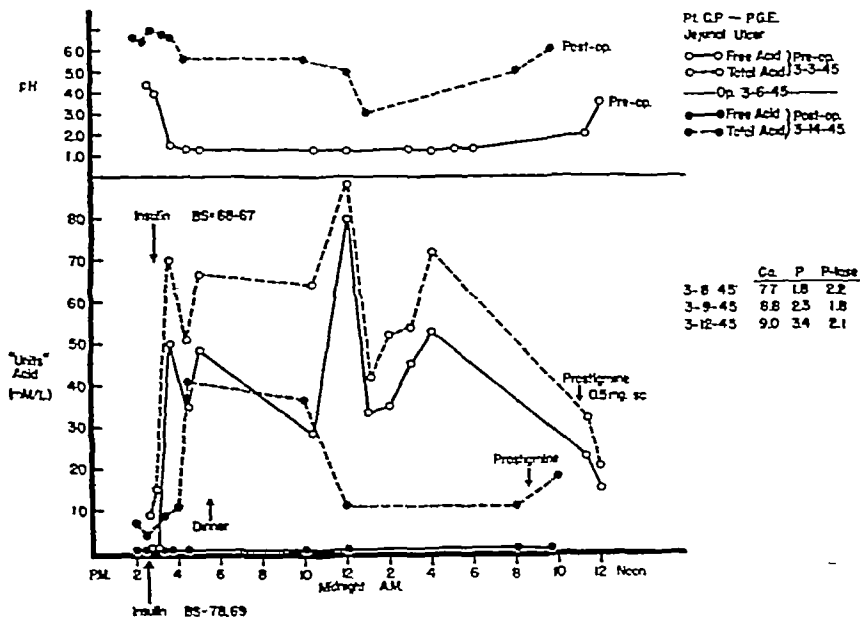


FIGURE 3 Charges in the Reactor and Titratable Acidity in Case 5 Preoperatively and Postoperatively

There was an increase in pH eight days after operation, as compared with the preoperative values. The titratable free acidity disappeared postoperatively, and the total acid was much reduced. A preoperative insulin test gave a marked outpouring of acid gastric contents (the blood-sugar levels are shown in the upper figures). A postoperative insulin test (shown below base line) gave no response, although the blood-sugar levels were in the same range. There was no significant change in reaction to prostigmine. Calcium values showed a fall immediately following operation, with a rise toward normal in the subsequent four days.

tained in all the follow-up studies so far carried out  
The typical secretory changes occurring preoperatively and postoperatively are shown in Figures 2 and 3. Similar data have been prepared for the

response in the unoperated stomach is so variable and so unreliable as to make this test a poor one  
The effects of insulin on gastric secretion have been mentioned by Weinstein et al<sup>42</sup> as being a

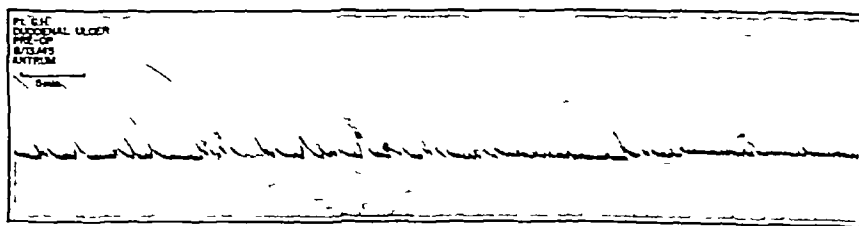


FIGURE 4 Motor Activity in the Gastric Antrum in Case 9 Preoperatively  
The large waves correspond to propulsive peristaltic activity and are normal antral waves

other cases and show essentially the same changes  
The secretory response to drugs has been of secondary interest, since it was considered that the unchanged secretory picture was the most important factor. The reaction to neostigmine has been studied because this drug may act by blocking the interaction between acetylcholine and cholinesterase. If the chief source of acetylcholine in the stomach — the vagus endings — were abolished, it is reason-

test for vagus section. They state that unless this reaction is abolished, the vagus nerves cannot be regarded as having been adequately sectioned. In these patients, studied postoperatively, there has been no insulin response. The preoperative insulin response was usually quite definite.  
The response to histamine is unchanged by this operation, which is as it should be. This response is probably a direct effect of the drug on the gastric

toms in our patients, and if this operation becomes generally applied, this phenomenon may be responsible for some poor clinical results. It is, however, of the greatest importance in selecting patients to avoid those who show complete obstruction due to scarring, both clinically and by x-ray examination. If they are so obstructed, either subtotal gastrectomy or posterior gastroenterostomy concomitant with vagus resection should be carried out.

Another interesting symptomatic result of this change in gastric emptying rate has to do with the completeness with which food is digested. Several

throughout the greater part of the twenty-four hour period. Some elevation may be observed an hour or two after the taking of food, but in general the patient goes through the day with no free acid. Second, there is a concomitant change in total acid, with reductions varying from 50 to 70 millimols per liter. Third, there is a change in total chloride content that roughly parallels this change in acidity but is not so marked. Fourth, there is a minimal change or no change in the total base concentration. Fifth, there is an increase of from 1 to 3 or more pH units at every hour during the day. We have

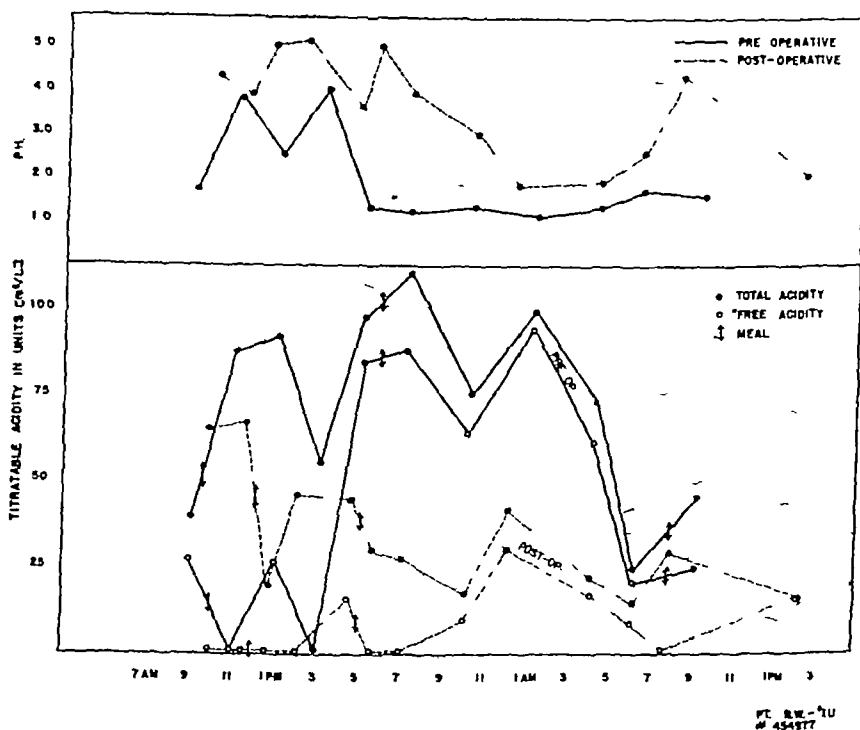


FIGURE 2 Chart Showing the Reaction and Titratable Acidity in Case 1 Preoperatively and Postoperatively

The postoperative tests were carried out approximately ten days after the operation. There was a rise in pH and a fall in titratable acidity following the operation, an alteration that has been maintained in follow-up studies.

of the patients have commented on the fact that, whereas preoperatively certain types of seed food, such as cucumbers and tomatoes, were poorly digested and often recognizable in the feces, postoperatively, regardless of what food is taken, complete digestion is secured and the stools do not contain undigested material.

#### Secretion

Effects on gastric secretion have been extensively studied and will be reported in detail in a separate paper. At the present time it seems sufficient to state that the immediate effects following vagus resection are as follows. First, there is a change in free acid values from normal or elevated to zero

seen no patients who following vagus resection showed a value below pH 1.5, whereas this is not infrequent in normal persons. In most patients with peptic ulceration the gastric acidity is in the region of pH 1.0, especially between midnight and 5 a.m. Lastly, the change in pepsin content has been inconstant and generally negligible.<sup>41</sup>

The standard procedure has been to leave the Levin tube in the stomach for eighteen to forty-eight hours, letting the patient be up and around the ward and allowing him to eat his usual meals without drugs or other artificial stimulation. This gives a picture of what is normally going on in the patient's stomach as nearly as it can be delineated with the patient in the hospital and with the tube

sensory change whatsoever has been produced. This leads also to the conclusion that vagus resection somehow alters the fundamental mechanism producing peptic ulceration.

Sensations of fullness, hunger or nausea are present following this procedure, according to the nature of the stimulus. Vomiting may occur if the

those described by Pfeiffer<sup>47</sup> in dogs following division of the vagus nerves.

We have done Graham tests before and after operation, and to date have found no distinct differences in the degree of emptying of the gall bladder.

Gastroscopy carried out preoperatively and postoperatively in Case 10 showed little alteration

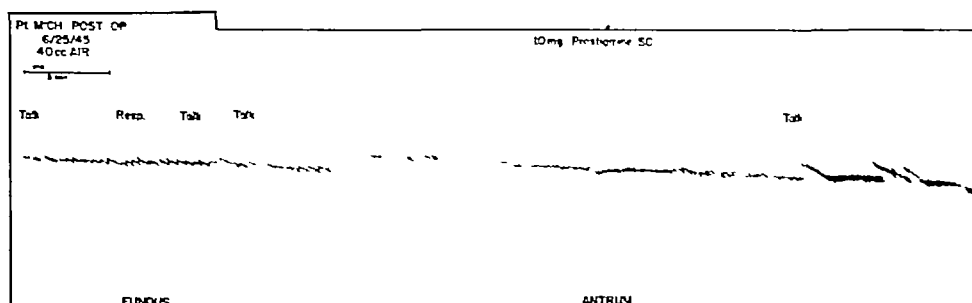


FIGURE 7 Motor Activity in the Gastric Fundus and Antrum in Case 7 Ten Days Postoperatively. Little motor activity was present, and there was no response to prostigmine.

stomach becomes overdistended, from which one may conclude that the normal afferent end of this reflex arc is also intact. Smithwick<sup>22,46</sup> has shown that many of the afferent pathways from the duodenum, gall bladder and biliary tract course the sympathetic nerves. The lower end of the esophagus, however, is not denervated from the sensory point of view by sympathetic ablation.<sup>46</sup> Nor does removal of the parasympathetic nerves at the level of this operation seem to alter sensation from the

save a decrease in reddening about the gastroenterostomy stoma.

#### SURGICAL TECHNIC

The surgical technic involved in this procedure will not be presented in full detail. A sizable segment of both nerves, running from the region of the lung root to the cardia of the stomach, is removed. We do this with the hope of interrupting fibers leaving the main trunks and entering the

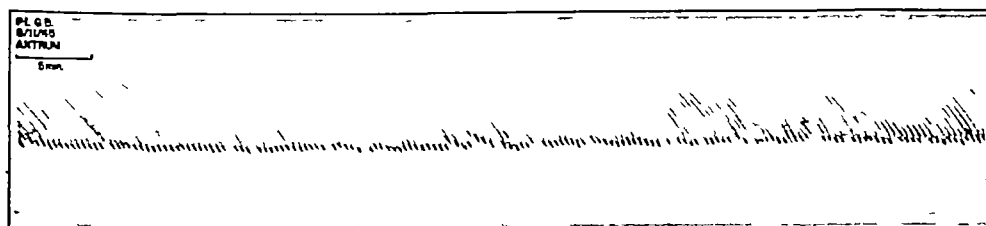


FIGURE 8 Motor Activity in the Gastric Antrum in Case 3 Seven Months Postoperatively. The so-called "automatic" type of motor pattern is quite different from that shown in Figures 4 and 6 for preoperative patients. It was observed in this patient many months after operation and makes a striking contrast to the earlier postoperative tracings, which showed little or no motor activity. This type of tracing may represent the local response of the denervated stomach to the stretch stimulus of a balloon in the antrum, unregulated by higher centers.

lower end of the esophagus. This indicates that this area and possibly the fundus of the stomach have sensory pathways that are not yet adequately described in human beings. A possible explanation is that the submucosal plexus in the esophagus continuously carries stimuli to the upper end of the esophagus before they pass out into the main vagal trunks.

Other side-effects of the operation are relatively few. There appears to be a lowering in the calcium concentration in the blood, followed by a rise to normal, these changes possibly being related to

esophagus that might possibly become expanded in their function to take over some of that lost by sectioning the main trunks. The diaphragm is cut to permit dissection of the nerves going to the stomach and is resutured between the severed nerve ends. The proximal ends of the cut nerves are encased in one silk cylinder, pointed cephalad and sutured to the pleura, which is closed behind them in a fashion not unlike that illustrated by Dragstedt.<sup>38</sup> Although the immediate physiologic results of both his operation and ours are doubtless the same, we have performed the more extensive

cells and is not mediated in any way, either by nerves or by other hormones, so that there is no reason to expect any change following an operation in which the gastric cells remain intact

### Motility

Studies on gastric motility have been carried out, and examples of preoperative and postoperative

not always long lasting, and in 1 patient waves of normal amplitude but abnormal pattern were observed eight months postoperatively (Fig 8)

### Pain

Changes in pain sensitivity to balloon distention have not been demonstrated in these patients to date. With the balloons in the lower esophagus,

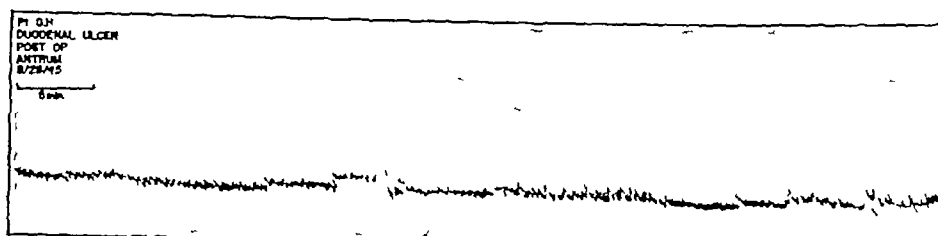


FIGURE 5 Motor Activity in the Gastric Antrum in Case 9 Eleven Days Postoperatively. This is a small portion of a long tracing showing a marked alteration in activity, which consists of the abolition of the large peristaltic waves.

tracings are shown in Figures 4, 5, 6, 7, and 8. These tracings have been secured by the use of an apparatus developed by Gorrell<sup>43</sup> and used extensively by Chapman,<sup>44</sup> which permits one to make accurate tracings of gastric waves by means of an electronic alternator and an electric motor that directs the recording apparatus in response to stimuli received from the stomach through a balloon tube. This

stomach, duodenum or jejunum, the threshold at which the patient experiences pain is correlated with the same degree of balloon distention preoperatively and postoperatively. This negative finding concerning sensory changes is of the greatest importance in evaluating the results of this procedure. In the dramatic symptomatic response produced in many of these cases, the patient awakes

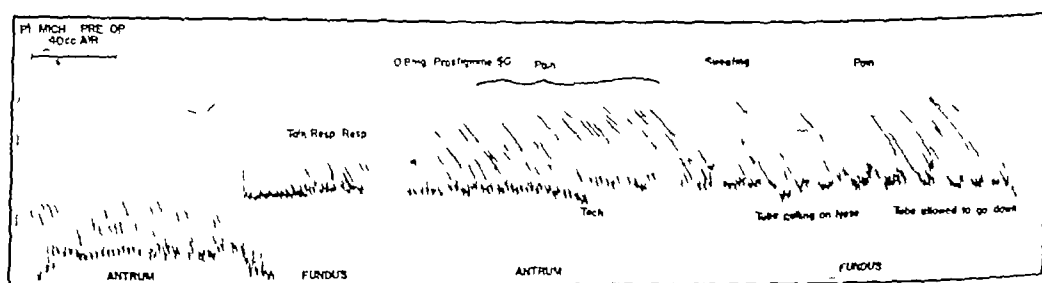


FIGURE 6 Motor Activity in the Gastric Fundus and Antrum in Case 7 Preoperatively. A motor response to prostigmine is observed, which was correlated with pain. The stomach tended strongly to propel the balloon downward, and there was an unusual amount of motor activity in the fundus.

device lacks many of the faults of other apparatus for gastric kymography in so far as extremely weak gastric contractions make an adequate tracing, and as a technical device it has been most useful. The intragastric position of the tube has been checked fluoroscopically in every case, an essential precaution since fundal activity is normally rather low.

The typical result produced by vagus resection in the early postoperative phase is the complete abolition of large gastric contractions. This is correlated with the change produced in the x-ray films, previously mentioned. There is a lessening of peristaltic activity. This effect is apparently

from the anesthesia stating that he feels that his ulcer has been cured or that he feels so well that he would never have known that he had had an ulcer. Such relief brings to mind the possibility that sectioning the nerves has simply anesthetized the stomach and duodenum so that the pain from continuing ulceration is not felt. The evidence against this conclusion, however, is overwhelming. The rapid healing of the ulcer, as well as the secretory changes, strongly suggests that a more profound change than anesthetization has been produced. Sensory studies demonstrate not only that the area is unanesthetized but that apparently no

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## AN INTERVIEW METHOD FOR OBTAINING PERSONAL HISTORIES\*

CLARK W. HEATH, M.D.†

BOSTON

**I**N MEDICAL practice, knowledge of the patient's personality and social history is often essential for diagnosis and treatment. There is great need both in practice and teaching for well organized methods of obtaining this information. The interview is a powerful instrument if properly employed, yet most students and physicians have received little training in the art of interviewing.

In recent years I have had personal experience with a short-interview method for the selection of officer candidates. This method, prepared by Woods<sup>1</sup> and designed to reveal pertinent facts regarding the man's capacities, interests, personality traits, weaknesses and strengths, does not employ an elaborate technical terminology and does not require psychiatric training. After a brief period of practice most interviewers who had an earnest interest in the variations of human personality could reach pertinent conclusions in the majority of young men examined. It seemed obvious that such a formalized, brief interview could be profitably employed as a means of obtaining the personal histories of patients. I have used some modification of it for most of my private and hospital cases during the last several years, and the experience thus gained has convinced me that an interview of this sort should be a part of the medical history.

The use of the interview embraces not only a certain technic but also a definite point of view. To illustrate this, 3 cases of borderline rheumatic fever in young adults will be cited. The histories and physical examinations were all much alike. There had been fatigue, malaise, probably some fever, and migrating joint pains. The fourth-year medical students, acting as clinical clerks, were quite properly concerned with the sizes of the hearts, systolic murmurs, temperature charts, white-cell counts,

sedimentation rates and electrocardiograms. In each case, brief questioning, following the plan of the interview, revealed within a few minutes some of the crucial facts needed for adequate understanding and handling of the illness.

The first patient was a high-school girl of sixteen years whose chief enthusiasm was for roller skating, in which she was possibly headed for a professional career. All her extra time and money were devoted to this absorbing interest, and she allowed herself only five or six hours of sleep. The second patient was a high-school boy of seventeen, whose history was much the same except that he was exclusively concerned with jive dancing. The third case revealed a more complicated personal history. The patient was a robust girl of seventeen who had been obliged to leave school two years previously because of the death of her parents and consequent financial restrictions. She lived with her grandparents, who assumed the role of Fagin. A brother was frequently confined in a mental hospital. The girl worked in a defense factory in the daytime and as a restaurant waitress in the evening, traveling for an hour by trolley between her places of employment. Her chief desire was apparently to receive a nurse's training, but this plan had to be indefinitely postponed because of the lack of a high-school education and the necessity of supporting her grandparents.

Obviously, the most important element in each of these cases was common to all — namely, abuse of the human machine, late hours and lack of sleep. Each patient required a somewhat different approach to correct the poor hygiene, necessitating a personal knowledge of the patient and mutual understanding between him or her and the physician. The medical students seemed to have missed this point, their training had not covered adequately the palpable relation of the social and personal history to the etiology of disease.

The term "personal history" covers a wide area. It is not sufficient to understand merely the tenets of psychosomatic medicine, as is illustrated by the

\*From the Grant Study, Department of Hygiene, Harvard University, the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) Boston City Hospital and the Department of Medicine Harvard Medical School.

†Physician to the Grant Study, Department of Hygiene, Harvard University; assistant physician Thorndike Memorial Laboratory, and assistant in medicine, Boston City Hospital; associate in medicine, Harvard Medical School.

operation for the reasons outlined in the introductory section of this paper

### DISCUSSION

The place that this operation will ultimately occupy in the surgical armamentarium is at present not clear. On the basis of our present limited knowledge and experience with the operation, little can be said concerning its limitations. It is clearly not indicated in acute perforations, acute massive hemorrhage or advanced cicatricial obstruction. These three situations should be dealt with by appropriate surgical maneuvers other than vagus resection. Beyond these obvious contraindications, we have not yet found criteria by which patients can be excluded from the possibility of benefit from this procedure.

The occurrence of bleeding in the past is no contraindication to the operation.

Gastric ulceration proximal to the pylorus should be approached with the greatest caution so far as this operation is concerned. The reason for this is that although the diaphragm is open, the region of the ulcer cannot be adequately visualized and palpated, and even if it could be, it is often impossible to differentiate ulcer from cancer. Resection should therefore usually be employed in such cases.

Patients who have had other surgery, such as pyloroplasty, posterior gastrojejunostomy or gastric resection, and who present themselves with renewed ulceration are ideal subjects for this procedure. The previous surgery does not in any way complicate the operation, and it may be carried out with excellent relief of symptoms in cases in which renewed attack on local structures through the abdomen would be technically complicated, with the end result open to question.

The largest group of cases in which this procedure seems to be of value is that of young or middle-aged men with a long history of peptic ulceration, possibly with previous perforations or hemorrhages, unobstructed and not acutely bleeding, who have been refractory to careful medical therapy and who have severe ulcer pain in times of stress,<sup>48</sup> which can be relieved transiently by the usual antacid, milk or food. This type of patient, in our experience, obtains a uniformly good result from this procedure, but the duration of the relief is at present unknown.

### SUMMARY AND CONCLUSIONS

The background and rationale of transdiaphragmatic resection of the vagus nerves for peptic ulcer is discussed.

This operation has been performed on 15 patients, and the clinical results in the first 12 cases are briefly discussed.

The general nature of the physiologic changes as regards secretion, motility, x-ray emptying and

afferent conduction follow a fairly consistent pattern and are described.

The operative maneuver employed is a trans-thoracic transdiaphragmatic resection of both vagus nerves in which a sizable portion of nerve is resected and steps are taken to avoid regeneration.

This procedure appears to be a potent weapon in dealing with peptic ulceration, as judged by clinical results in these early follow-ups.

The final value of this method must await the passage of time and careful study of the patients operated on at this and other clinics.

It is hoped that radical transdiaphragmatic resection will avoid the return of the ulcerating tendency, which stands as the chief obstacle to the success of this or any other operation for peptic ulcer.

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sequent topics such as athletics, activities and interests and the choice of a career. Particular interests and abilities are easily elicited through the patient's choice of subjects and his liking for or dislike of particular courses.)

#### A Scholastic

How old were you when you left school?  
How far did you get in school?  
What high school (college) did you go to?  
Did you like it there?  
What subjects did you like best?  
What did you major in?  
Why did you choose that field?  
Did you do all right in mathematics? (English, etc.)

#### B Extracurricular Activities (The choice of a field of specialization in college may lead naturally to a choice of lifework. If so, the following questions may be deferred until later.)

What did you do outside of courses in school (college)?  
Did you receive a scholarship?  
Did you have to earn some of your way?  
Did you go out for a school paper? Glee Club?  
Special organization?  
Did you hold any offices?

### III Activities and Interests (The examiner should strive to get an estimate of the patient's muscular co-ordination and ability to withstand strenuous exercise.)

#### A Athletic Activities

Did you spend much time in sports?  
What sports do (did) you take part in?  
What was your best sport?  
Were you on a varsity team?

#### B Spare Time

What do you do in your spare time?

#### C Outdoor Life

Do you like outdoor life?  
Do you swim? Fish? Hunt? Sail? Ski?  
What experience have you had in hiking? Camping?

#### D Summer Activities

What do you like to do summers?  
How do you like to spend vacations?  
What did you do last summer?

#### E Artistic and Special Abilities

Have you any special hobbies?  
Do you play a musical instrument?  
How much training have you had in this?  
Do you sketch or draw?  
Do you like to read?  
What books or magazines do you like to read?  
Are you handy with tools?  
Do you drive a car?  
Can you repair it?

#### F Social Activities

Do you have many close friends?  
Do you find it easy meeting new people?  
Do you prefer to do things with people?  
Do you and your wife dance?  
Do you play cards?

### IV Family Life

#### A Boyhood Home

What was your father's occupation?  
What was your father like?  
Did your mother have an occupation outside of her home?  
Were you close to your parents?  
What about your brothers and sisters?  
What are they doing now?

#### B Married Life

How old is your wife?  
Where was her home?  
Does she enjoy housework?  
Does she have interests outside of the home?  
How long did she go to school?  
How many children have you?

What are their ages? Sexes?

Do they ever get on your nerves?

How do you and your wife spend the evenings?

Are you and your wife of the same religion?

How do you get along together sexually?

### V Religion

What is your religion?

Were you brought up in this religion?

Do you belong to a church?

How important is your religion for you?

Do you enjoy ritual?

Do you send your children to Sunday school?

### VI Occupation (The manner of choosing a career and the motivations that impel a man in his work are sometimes the richest source of knowledge concerning him. The opportunity also may be taken here to determine the actual duties at work, so as to discover possible occupational hazards and strains bearing on the illness.)

What is the nature of your work?

How did you get into this field of work?

Does it satisfy you?

Do you get along well with the people there?

Where do you think your abilities lie?

Do you seriously consider some other field (teaching, law, business, etc.)?

What are your plans for the future?

### VII General Habits

What time do you usually get to bed? Get up in the morning?

Do you smoke? Drink? Take any medicines?

Are you naturally orderly with your things?

What do you usually do when you get home at night?

### VIII Mood (Minor mood swings, without necessarily being pathologic, are frequent, and are sometimes responsible for unexplained variations in efficiency. Moreover, the mood in some persons seems to be set at different levels — some being naturally warm and optimistic and others depressed and pessimistic.)

Do your spirits run on an even keel?

Do you run into periods of a week or so in which you are not so efficient, or do not feel so well?

Do you have any trouble in controlling your temper?

### IX Stability of Autonomic Functions

Does it affect you to have to speak in public?

In college were you affected by examinations? Games?

Are there any particular stresses that cause symptoms?

Does anything interfere with your sleeping? Eating?

Does anything ever produce diarrhea? Frequency of urination?

### X Over-All Judgment of Personality and Recording of Personal History

The judgment of the patient's personality\* is made from the interpretation of the answers to the above and similar questions and from the appearance, manner and expression. The personal history may be recorded in simple language, since it bears on the complaints and the medical diagnosis in question. A good deal could be said for placing it as a preface or foreword to the formal medical history.

\*No attempt is made to suggest a formal personality classification. For the purposes at hand it seems best to describe patients in words of every day language such as "dependable," "reliable," "likable," "mature," "well-mannered," "straightforward," "cheerful," or their reverse "an energetic, hard-headed businessman," "a neat, precise rather sensitive individual" and so forth. Some attempt should be made to record what in the opinion of the doctor is the strength of the material the patient is made of: that is, is he basically sound, invulnerable and well-integrated? Are his problems the result of circumstances or relatively self-conditioned? Description of the person naturally seems to divide itself into constitutional and basic traits, more environmentally conditioned or temporal traits such as education, career choice and manner of life and environment, including family, friends and physical conditions. These factors may be recognized to form a system, each playing a role and impinging on the nature of the illness and the therapeutic indications. A discussion of personality classifications will be found elsewhere.<sup>67</sup>



many authenticated cases of the relation between mind and physiologic function. Before these factors can be adequately evaluated, there must be an understanding of the patient as a person and of his environment and systematized knowledge concerning not only the relation between mind and body but also that concerning personality and its role in the environment. The present report has to do with the latter and is necessarily only an introductory statement. The term "personal history" embraces not only the personality but the social history, as incorporated in medical-history forms, as well as some part at least of the traditional items in the family history, marital history, occupational history and habits.

#### GENERAL ASPECTS OF THE INTERVIEW

The task in obtaining the personal history is not only to acquire a working knowledge of the personality of the patient, his activities and interests and his environment but also to establish a satisfactory physician-patient relation so that immediate therapy and future handling of the case will be facilitated. Much has been written about this sort of approach, which is the very core of the practice of medicine. Monks<sup>2</sup> in a pertinent article written in 1939 drew on the experience of Roethlisberger and his co-workers<sup>3</sup> for practical suggestions in the technic of interviewing. The latter have pointed out that the interviewer is in the role of a listener, who "should listen not only to what a person wants to say but also for what he does not want to say or cannot say without help." A book by Bingham and Moore,<sup>4</sup> entitled *How to Interview* gives excellent material for the technic of various kinds of interviewing and describes their dangers and pitfalls.

The interview is appropriately a part of the medical history. Brief questions are asked, giving the patient the opportunity to expand his replies. The approach is clinical, but it differs from that of the rest of the clinical history in an important respect. Whereas the usual clinical approach is to explore the range of possible diagnoses, the purpose here is to reveal positive traits and capacities and to discover what the patient does and likes to do and the nature of his background and adjustment, his way of life and his occupational and cultural environment. Some reorientation is necessary in the physician's thinking in acquiring this kind of information, for his training in history-taking, particularly if he has just completed his medical-school and hospital training, has been largely in the direction of identification of disease. The personal history serves a double function, since disabilities and defects inevitably come to light in the course of a well handled interview, and their nature can be pursued by appropriate questioning. Nevertheless, the main intent of the personal history should be to learn "the whole nature of the man within the patient."<sup>5</sup>

The physician should have either in mind or close at hand on paper a suitable outline of the kind of information he wishes to obtain. This varies somewhat, depending on the patient's age, sex, intelligence and cultural background. Competent interviewing is an art that is developed by experience. It is materially aided by a pertinent and thorough plan of the field to be covered. A suggested outline of topics and appropriate questions is given below.

It is a mistake to follow rigidly any definite order of questioning. Certain questions strike home in certain patients who, if they believe that they have a sympathetic listener, describe conditions of their life that are extremely revealing. In such cases, the order of the interview should be dropped for the time, the patient being allowed to pursue the point in question until the examiner is satisfied that a satisfactory understanding of the situation has been reached. The physician should be constantly alert to such possibilities. Here, as elsewhere, the advantage of the clinical method lies in its flexibility and its adaptability for different persons and changing circumstances. It has been observed that one must listen not only to what the patient says but for what he does not say. Often it is the manner in which a question is received and answered that is of importance rather than the actual content of the answer. To adopt the expression of Woods,<sup>1</sup> "The interviewer must depend upon the astute use of all his senses rather than upon systematized appraisal of question and answer." Diagnosis in this field has not advanced nearly so far as has the recognition of classified somatic disease. Nevertheless, even in the latter field, reaching a diagnosis is often somewhat more of an art based on broad experience than it is a technic.

#### OUTLINE OF INTERVIEW.

The following list of suggested topical headings is necessarily only tentative and is not to be rigidly followed. Limitations of time and the particular circumstances of the patient alter the pattern. The questions listed under the various topics are merely introductory ones, and should be altered to suit the circumstances. They comprise those that seem likeliest to elicit revealing answers. Answers that are suggestive should be pursued by questions of a like nature. For the purpose of illustration, it will be assumed that the patient is an adult man who has had a college education, is married and has held a job for a number of years. Questions inappropriate for the person who has not attended college, for the single person or for a younger man will naturally be eliminated, and others may be substituted.

- I *Appearance and Expression* (At the start a mental note is made of such items as general appearance, body build, dress and temperature and moistness of the hands, and throughout the interview expressive movements and the manner of speech are observed.)
- II *Education* (The educational history offers an easy approach to the interview. It naturally blends with sub

A Good, and we have found use for it I bought a single-family house five years ago Had a setback on it a couple of years ago and I had to mortgage it, but since then things have gone easier Still paying on the mortgage

Q What is your actual income?

A Basic income from school is \$4000 with the emergency allotment. It would be about \$3880

Q Do you have a car?

A Yes, I own a car and drive it

Q Do you feel you had to work this summer?

A I felt I wanted to after buying this cottage — a duplex The income from the one half will more than take care of the other once I get by this primary arrangement

Q But you could have gotten by without working?

A Yes

Q What do you do with your spare time?

A We lead a rather quiet life We have five children, the last was born just last July Haven't had too much occasion to get out and do things We get along rather nicely, but we don't have activities programmed out We have many friends, and although we haven't been going many places because of my wife's condition, we are not antisocial, and when time permits, we visit.

Q Do you and your wife play cards?

A We play when we have to, but we don't have time

Q Do you read much?

A. Not much [Named two current magazines] Nothing much Of course, I read a good deal in my line of work I study everything for accounting and teaching, but I like fiction

Q Listen to the radio?

A Yes, but not too much

Q Ever go dancing with your wife?

A. Yes, on occasion, but there are few lately I'm an emotional cuss, I guess I wouldn't be happy if I didn't push myself My wife recognizes this, and tries to restrain me only to a certain extent

Q Do the children get on your nerves?

A Yes, very much at times But you love them just the same. We really get along very well They are sore at me right now for not coming home I'll have to fix that up

Q What is your religion?

A. Catholic.

Q About how strong is the influence?

A. Strong influence, devoted to the church and go regularly Follow the religion

Q And the children?

A We raise them accordingly

Q Are the children doing well in school?

A. Very bright, the oldest is just past 5, started last year in kindergarten and is in the first grade this year We were told that he was one of the best down there. The girl following him is in kindergarten now We had our fifth youngster in July

Q Has there been anything in college or school such as examinations which got you upset?

A Maybe in the beginning, but not so much later I try to divorce the idea of confidence from concert. I feel I have something that I should not be afraid to approach anybody on There were some times when I got gas and used to shiver

Q What symptoms did you notice when you were young?

A. Sour stomach and gnawing at night.

Q Any effect on the bowels?

A. No

Q Did you think it affected passing water?

A The frequency of the passing of water increased

Q Did examinations bother you?

A. No, I would get keyed up, but no more than the average person Might find that perhaps I was not ready for it, but normally I took it as it came along except for the usual emotional turning up that everybody gets

Q When you are nervous, do you smoke more?

A Yes, this is one of my big weaknesses Don't care much for cigars, especially what they are handing out these days [He smokes six or seven cigars a day]

Q What about eating?

A I eat fairly fast

Q Now, you sleep well, do you?

A Yes, prior to this little disturbance now Within the last 2 months I have been waking up nights I have had the vision of this thing coming on Guess it's because I'm a teacher I can understand my situation I figured on this particular situation With the type of operation I had, I knew it was not one that would be a permanent one with me, particularly since my sister, who had a complete stoppage 2 years ago, had the more recent type of operation in which they removed two thirds of her stomach I thought it would come to me

The interviewer in this case spoke less than one fifth of the time The questions kept clear of strictly medical symptomatology and were directed toward what the patient did, could do and liked to do, how he conducted his life, what his interests were, and to some extent the influence of his way of life on his bodily functions The interviewer was not under the necessity of making a psychiatric diagnosis An academic classification of the personality would have been of accessory interest The problem was the simple one of determining what factors in the patient's life had to do with his illness, the better to advise him and to arrange conditions to help him to live with health and comfort

Advance in knowledge of the psychosomatic field may clarify such an approach, but the problem must always remain that of getting to know the patient and his environment in order to treat him more effectively There is need for adequate classification in this whole area so that the usual social and personal factors bearing on particular illnesses may be more easily recognized The particular point considered here, however, is the technic of interviewing, so that it is preferable to describe the patient in simple, nontechnical language In the case just cited the personal history might be recorded somewhat as follows

This is a tall, rather heavily built, dark-complexioned man who is very co-operative and talks rapidly He shows little anxiety He is a college teacher of accounting and the father of five children On the side he does real estate work His religion is Catholic, but he does not seem to be deeply devout In fact he has no great depth of thought He is intelligent, pleasant, energetic but without many resources within himself He is happiest when he is on the go He says that he leads a quiet life, yet his fifth child was born recently, and his real estate ventures outside of an active career of teaching give him no leisure Perhaps his restlessness is related to his poverty in his youth and the necessity to seek financial security, which seems to be a strong motivating force in his life He has many strong basic qualities, such as reliability, dependability, persistence and conscientiousness He is rather simple, accepting life as it comes, and yet is not unaware that his periodic gastrointestinal illnesses are in some way linked with his continuous, restless activity One has the not unfamiliar impression of a man of affairs restlessly pursuing his career at fast tempo — hardly an ideal way of life for the patient with peptic ulcer and one that quite likely can be of etiologic significance

The patient was convinced, before the discussion took place, that he should receive partial gastrectomy particularly since a sister was apparently treated successfully in this manner He believed that he could thus continue symptom-free and

The simple factual material may be recorded as usual in the traditional medical-history outline, under headings such as "Family History," "Marital History," "Social History," "Occupation," and "Habits." A chronological handling of the personal history is often of value, for it may illustrate the sequence of events or repetitions of them that bear on the present illness. If the statement is sufficiently descriptive, it will serve as a personality judgment itself and will be of some prognostic significance.

In respect to women patients, suitable alterations of the questions listed above will suggest themselves. The lifework is usually of lesser importance. Family life, social life and interests, and abilities in the household arts are among the more profitable topics to pursue.

### A TYPICAL CASE

The following is an abbreviated account of an interview with a patient suffering from a bleeding peptic ulcer, recorded verbatim. It will be recognized that liberties have been taken with the above outline, for brevity's sake only the most pertinent facts being included. Taking notes is not an ideal method, and it is often difficult to recapture the feeling of the interview through the written record. The interview illustrates, however, the simple, direct method of questioning following a plan. The patient was quite willing to discuss at least the superficial activities of his daily life and some of his accomplishments and aspirations.

L. H., a 39-year-old, married schoolteacher, was admitted to the Medical Ward on September 8, 1944. Symptoms of peptic ulcer had been noted since he was 20 years of age. At 22 years, he was operated on for so-called "perforated duodenal ulcer." At 29 years, there was an episode of weakness and black stools. At 33 years, there was a severer attack of bleeding, with hematemesis. Bleeding occurred a third time at 37 years. During the 2 months previous to admission the patient had eaten irregularly, and for the last 5 days he had felt weak and tired. Three days previously, he began to pass tarry stools. A sister had peptic ulcer, which was operated on, apparently successfully, by partial gastrectomy. The patient desired this operation for himself, hoping to return to his customary activities.

Physical examination revealed a tall, heavily built man, pale but in no discomfort. Examination was otherwise negative. The red-cell count was 3,050,000, the hemoglobin 56 per cent and later 45 per cent, and the hematocrit 26 per cent. A blood smear was negative except for hypochromic red cells. The urine was normal. The nonprotein nitrogen was 45 mg per 100 cc. and total protein 5.5 gm. A blood Hinton test was negative. Guaiac tests of the stools were strongly positive.

The interview was as follows:

Q How much schooling have you had?

A I had my public-school training at ——— High School and then worked for 4 years. There is where I made my first mistake, but it turned out all right. After working for 2½ years I started with evening courses at college. After 1½ years of that I dropped the day work and went to college as a regular day student.

Q How old were you when you finished high school?

A Sixteen when I finished high school, 17 shortly afterward.

Q When did you finish at college?

A January, 1927.

Q Did you have to earn your way through college?

A Just my board. My father died when I was an infant. My mother kept the family alive. She's still living.

The decision which I made to return to college was influenced by the decision of the family.

Q Did you engage in extracurricular activities while in college?

A Yes, I was elected two years running to fraternities, but I did not have much time.

Q What about sports?

A I liked them, but never participated. Never seemed to have time, except for sand-lot activities. I was really very busy all the time due to family circumstances.

Q Did you get good marks in school?

A In high school I "slowed off" as I was working after school and had no thought of going on to college. Did fair work in high school.

Q What about camping and outdoor activities?

A None, except last summer I had a cottage at ———, where there were ample facilities for such things, and I thought my wife and I could have a lot of fun out there. I expect to buy a sailboat or motorboat.

Q Do you like that sort of activity?

A Yes, and the youngsters would get a kick out of it, too.

Q Are you mechanically inclined?

A No, I'm not mechanically adept.

Q What about musical activities?

A I started on the violin, enjoyed music, but I haven't had the time to go into it too much. I've done some tax work for several musicians in an orchestra and thought I should look into whatever it was that made them so interested.

Q What were your plans after high school?

A I went to work at the American Telephone and Telegraph Company when I left high school.

Q You were thinking of something in business?

A Yes, I was there for at least three years. Then I resigned from there to go with Procter and Gamble. I was disappointed there and would have been far better to remain with the telephone company.

Q Any degrees from college?

A B.S. and M.A. degrees from college. I did much better there than in high school.

Q When did you start teaching?

A I started to teach there. Professor ———, head of the ——— Department, started me teaching. He was more or less of an inspiration to me and brought me into the ——— Department as his own corrector, and my last year there I was an assistant instructor, and then following that they sent me to the University of Puerto Rico to teach accounting.

Q Did you go to Puerto Rico?

A Yes, I taught one academic year, about 9 months, teaching bookkeeping and accounting there, then I came back here to teach.

Q Do you think your abilities lie there?

A I do seem to feel that in general I have been able to get along very well with people and don't have very many enemies that I can think of. One examiner in the Boston schools said I was a born salesman. I have perhaps brought that up a little bit by my side activities in real estate.

Q What were these side activities?

A I set up desk space over in ———, a real estate office. Because of my teaching course I would not be there in the daytime, but I managed more or less to work into the real estate activity.

Q Did you like it?

A I don't know whether I would like it as a full-time venture. The head of it spoke to my wife and said I learned more about it in a year than most people do in fifteen or twenty years. Perhaps that's because I was interested in it as a side venture.

Q Have you been successful in selling in that sort of field?

A I have. For example, I just went in there more or less to maintain my desk space that summer, and before I officially closed my season, I sold three or four houses. The next year I doubled my sales, but this year I didn't do so much on account of my illness.

Q What is your family income?

problem more quickly resolves itself into one of adjustments or of personal hygiene. Garrulous and uerulous patients are of course encountered. In such cases time and patience are most needed, but one may be helped by dropping a subject and going on to one of equal interest to the patient. Patients vary in the orderliness of their answers, yet they nearly always care for the physician's time, particularly if they recognize his genuine efforts to try to help. Most patients are honest and describe symptoms, worries and fears that are real to them. It has perhaps been overemphasized by psychiatrists that illness is sometimes a means of avoiding unpleasant situations, but it is rare to find definite proof of this mechanism. Perhaps, like hysterical episodes, it has become less frequent than formerly. Today the social and personal concomitants of disease seem to come under the heading of satisfactions and dissatisfactions — in other words, adjustments. Successful interviewing requires a spirit of trust in the patient. At the same time, if the physician will take the time to delve into the positive qualities of good, he will find a most helpful adjunct to his success in the practice of medicine.

#### SUMMARY

A method of short interviewing for obtaining personal histories is outlined. It consists of short, pertinent questions, covering the positive qualities,

activities and environmental relations, the patient being given an opportunity to talk freely. Examples of questions and a sample interview are given.

It is believed that an adequate personal history should be a part of formal medical history-taking. Students should be thus instructed.

The lack of adequate attention paid by medical teachers and practicing physicians to the more general personal and environmental facts of patients' lives is related to the one-sided development of technical knowledge and specialization, symptomatic of the times.

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pursue his accustomed mode of life. One wonders, however, what would be the ultimate effects of such a strenuous life apart from the success of the gastrectomy. Up to nine months postoperatively this patient was free of gastrointestinal symptoms, and he had managed to free himself of many of his outside activities.

\* \* \*

The concept of the physician as friend and adviser of the patient goes back to ancient times. The point of view has been expressed well by modern writers.<sup>8,9</sup> There is nothing new claimed for the material presented here, including the interview method itself. Many physicians with experience in general practice recognize the importance of a personal knowledge of the patient, and they have developed their own technics for managing the patient in some manner analogous to that described. It is therefore surprising that the study of personality and environment forms such a small part of the teaching of medicine. It is as though this teaching were planned to train students for only half their probable duties as physicians—the more technological duties. The physician cannot confine himself to his technological last without harming many patients. Looking at the matter from a broader point of view, one gains the impression that the concentration of medical curriculums on the more specialized branches is symptomatic of what has been occurring in the world outside of medicine. Mayo<sup>10</sup> writes

He is an inveterate optimist who is not sobered by a comparison of our own time with the high expectations of a century ago. In no area of activity have nineteenth-century expectations been disappointed. But privation and strife have not vanished from the earth. *While material efficiency has been increasing for two hundred years, the human capacity for working together has in the same period continually diminished.*

Perhaps the capacity for working together has not changed so much, but the conditions that affect it have altered greatly. The human capacity of physician and patient for working together has been affected by the tremendous growth of specialized knowledge in the medical sciences. There are few physicians who will deny this, yet disproportionately little interest is being paid to this essential aspect of medicine. Little enough is known in this area, at least compared to the body of established fact in physiology, pathology, bacteriology and the like. Medicine could benefit in this direction by closer contact with some of the other disciplines concerned with the welfare of people, such as physical and cultural anthropology,<sup>11</sup> clinical psychology, education and the social sciences.

A step toward the desired goal would be to introduce as a required part of history-taking an adequate survey of the personal facts about each patient. This would not only be of educative value to the student but would also inevitably direct

closer attention to the gaps in one's knowledge of people. Through interested teachers a body of data could be accumulated for investigative purposes that would allow medicine to contribute a greater share to the knowledge of personality and environment and their relation to the total social scene.<sup>12</sup>

This approach is not without therapeutic value. All patients naturally have a primary interest in themselves and their affairs, and most of them are ready to talk if the circumstances seem appropriate. They often have no one with whom they can discuss their problems. Unfortunately, many believe that most physicians are interested only in such factors as physical examination and physiologic mechanisms and tests. Many patients show some insight into the personal or environmental side of their illnesses, which may be the seed for better self-understanding. It is well known that the latter may come not so much by direct advice from outside as by a kind of self-education from within. Traditional medical history-taking searches for what is wrong. A better balance and a more agreeable approach for the patient are brought about by the addition of the personal history, which emphasizes not so much what is wrong as what are the positive qualities. Medical case histories if taken at their face value paint dismal pictures. The pessimism that they depict is not thereby closer to the truth.

The personal interview helps to decide the essential question as to whether the matter might not be better handled by a psychiatrist. But most patients do not need a psychiatrist, advantageous as this might be. The friendly counselor, which the physician should be, is quite as competent as the psychiatrist to handle the large proportion of problems presented by private patients, and he is sometimes more so. Many psychiatrists freely admit this. Moreover, there are not enough psychiatrists to care for the large numbers of patients who have symptoms not referable to organic disease. The essential point is to know when the psychotherapeutic problem can be better and more safely handled by the specialist.

There have been certain objections to proposals for spending time and effort in exploring the personal history of the patient. Many physicians fear to encroach on areas of an intimate nature, but most patients readily understand what the physician is driving at in the interview. Involved questions may arouse a fear that the physician has mental disease in mind, but this fear is dissipated by simple questions about school, choice of work, family, friends or some point the patient himself has raised. On the other hand, if mental disease is present, the problem must inevitably be gone into.

The question of time-saving is always an important one. In the majority of cases there is actually a large saving of both the physician's and the patient's time. Useless referrals and unnecessary tests and appointments may be avoided when the

Since there was likelihood of further air raids, with subsequent difficulty in controlling the patient, it was decided to evacuate him to a hospital in a quieter locality. At about the time the patient was scheduled for evacuation, 4 days after the atropine dosage, he suddenly became alert and rational. When he learned that he was to be evacuated, he said that he remembered nothing of his activities during the last 4 days. When told something of what he had done, he apologized and asked that he might remain in the hospital rather than be evacuated, since he wanted to return to duty with his own organization. He was amenable to all forms of treatment. Later on the same day he first began to show slight sweating of the skin and his pupils began to react lightly to light.

On the following day, psychiatric examination showed good rapport, with normal emotional responses. There was no evidence of delusional thinking or hallucinations, in fact, the latter were not reported at any time during the psychotic episode. The patient showed complete insight into his previous paranoid delusions. He stated spontaneously that during the active period of the psychosis he had aroused momentarily, realized that his thinking was abnormal and then lapsed into his previous state without being able to help himself. There were moderate sensorial defects — that is, in orientation, recent memory and simple calculations.

The following information concerning the patient's background was obtained. He was an average, outgoing youngster, the sixth of 11 children. Throughout his schooling, which took him through the ninth grade, a year in the Civilian Conservation Corps, 2 years of steady work in a coal mine and his period of service, he was sociable, athletic and extroverted. The family relationships were normal. His direct antecedents showed no neuropsychiatric abnormalities. Both by history and by direct observation the patient's total personality development was the polar opposite of paranoid.

During the next 3 days, the patient was kept under moderate sedation with phenobarbital. In spite of the fact that there were other air raids, he was calm and composed during each one, showing no tendency to become maniacal or even excitable. The pupils became smaller during this time, approaching normal size 7 to 9 days after he had been given the atropine. He also noticed that his power of accommodation improved.

On November 1, the patient felt perfectly normal. He was re-examined neurologically and psychiatrically. The psychiatric examination showed continued complete insight, and rapport and sociability were above average. The sensorial defects previously noted had entirely cleared. General comprehension was good, arithmetical reasoning fair,

understanding of similarities and contrasts good, memory for a story in one paragraph good, and vocabulary fair, and he was able to repeat eight digits forward. Intelligence was estimated as low normal, and the defects previously noted were therefore regarded as significant and as related to the toxic action of the drug.

The neurologic examination was also normal except for slight hypesthesia over the distribution of the right saphenous nerve. At the height of the acute psychotic episode the patient had received a contusion on the inner aspect of the right thigh. It was believed that this explained the slight subjective sensory abnormality of the right saphenous nerve. The patient was discharged to duty 2 weeks after the onset of his illness. He was normal in every respect and anxious to return to his old assignment.

## SUMMARY

A case of severe poisoning following the ingestion of 10 gm of atropine sulfate is reported. The patient made a complete recovery in two weeks. This was punctuated by a brief but violent psychotic episode, consisting of confusion and paranoid delusions, in a person of basically normal personality makeup. The psychiatric improvement was concomitant with the first signs of sweating of the skin and reaction of the pupils to light. When discharged to duty, the patient showed perfect insight into his previous toxic psychosis.

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## CLINICAL NOTE

## ATROPINE POISONING

REPORT OF A CASE, WITH RECOVERY AFTER THE  
INGESTION OF ONE GRAM

CAPTAIN EBEN ALEXANDER, JR, MC, AUS,  
MAJOR DONALD P MORRIS, MC, AUS, AND  
RALPH L ESLICK, PA SURG (R) USPHS

THE effects of atropine when given in therapeutic doses are dramatic. When it is given in doses that may cause poisoning, the results are sometimes extremely serious or even fatal. The exact incidence of such poisoning is not known. Deaths from this cause constituted an extremely small percentage of those from poisoning in Massachusetts from 1928 to 1937 — considerably less than 1 per cent.<sup>1</sup> There are several reports of cases of poisoning and of recovery with doses of atropine varying from 0.4 to 100 mg.<sup>2-7</sup> In each of these cases the reaction followed a distinct pattern, the differences between the cases being one of degree rather than of variability of reaction. The largest dose of atropine given with subsequent recovery is apparently that reported by Comroe,<sup>2</sup> whose patient received 0.5 gm by mouth.

In several of the cases mental disturbances were evident.<sup>3-5, 7</sup> These consisted of transient confusion and visual hallucinations. The patient in the present case, on the other hand, showed confusion and paranoid delusions, without visual hallucinations. His behavior was also much more violent than that of the others. This difference may be related to the large dose.

In view of the fact that this patient received twice the maximum dose previously reported, and in view of the differences in the psychotic reaction, it is believed that a summary of the clinical course will be of value and interest.

## CASE REPORT

A 23-year-old man of Polish extraction complained, on October 22, 1944, of severe abdominal pain, which necessitated calling the medical officer. The officer had seen him 6 months previously when he had a similar attack of abdominal pain. At that time he was sent to a hospital, where he recovered completely without benefit of operation or special x-ray examination. The appendix had been previously removed. He returned to duty and performed his duty satisfactorily until the reoccurrence of the abdominal pain.

At examination the abdomen was held somewhat rigidly, but there were no masses and there was no localized tenderness or spasm. The medical officer administered 16 mg of morphine sulfate subcutaneously and instructed his assistant, an enlisted man, to give 0.4 mg (1/150 gr) of atropine sulfate but the latter through error gave 10 gm (15 gr) of atropine sulfate by mouth. This was contained in a small

ampul (Merck — Atropine Sulfate, U.S.P. Powder, 40's). There was no doubt that the patient consumed the entire dose, and he was not seen to vomit at any time after its ingestion. The size of the dose was well attested to by the medical officer in charge, who later brought to the hospital an ampul of atropine sulfate exactly similar to the one that had been given to the patient.

Within a short time the patient began to feel hot and flushed and complained that he could not see well. In the course of the next 2 hours, he became stuporous and difficult to arouse. Two hours after he had received the atropine, the stomach was washed out with a weak solution of potassium permanganate. During the next 24 hours the patient became comatose, the pupils dilated widely and were not responsive to light and the temperature rose. The respirations became increasingly slow and shallow, and at the end of 24 hours were so shallow that the patient appeared not to be breathing, but the pulse remained rapid and regular. He was given supportive therapy, including 5 per cent dextrose in 2000 cc of water, and showed some improvement, and was then transferred to an Army evacuation hospital in an extremely critical condition.

The temperature was 104.2°F, the pulse 110, the respirations 20, and the blood pressure 101/60. Physical examination revealed a well developed and nourished man in a stuporous state who reacted only to very painful stimuli. The skin was extremely flushed and hot and perfectly dry, with no cyanosis. The heart, lungs, abdomen and extremities were normal. On neurologic examination, the pupils were extremely dilated and did not react to light. There was a bilateral external strabismus, and the eyes were not attracted by a moving light. The fundi were normal. There was no facial weakness. There was slight but not marked stiffness of the neck, with a mildly positive Kernig's sign. The deep tendon reflexes were bilaterally diminished but equal. The abdominal reflexes were diminished, and the cremasteric reflexes were equal. The Hoffmann sign was normal bilaterally. The Babinski and Chaddock reflexes were unequivocally positive bilaterally.

A spinal puncture was done, with the following normal findings. The initial pressure was equivalent to 160 mm of water, and the cells were not abnormally increased. No facilities for determination of the protein or gold-sol curve were available.

Within 1 hour of admission, or 30 hours after the atropine was given, the axillary temperature was 105.2°F. Alcohol sponge baths reduced the temperature to 102°. Two thousand cubic centimeters of 5 per cent dextrose in water was given by vein and during the next few hours he voided several times, each time using the urinal. He was not incontinent. The urine showed no abnormality except for the presence of sugar, which was accounted for by the dextrose received by vein. Subsequent examinations showed no sugar.

On October 24, 40 hours after the dosage of atropine, the patient began to react. He knew his name but did not know where he was or the date. The temperature was 99.0°F, the reflexes were normal, and the Babinski and Chaddock signs were negative. The pupils were still widely dilated and showed no reaction to light. The patient was unable to accommodate his vision. There was no sweating.

On October 25, the patient was apparently improved. He was tremulous but co-operative and seemed rational. The temperature and reflexes were normal. He was restless. In the and was given mild sedation with phenobarbital. In the evening of this day, during an air raid, he suddenly became maniacal, began to scream, stripped off all his clothes and ran about the hospital. He was restrained with great difficulty, and was sure that all those trying to return him to his bed were his enemies and were trying to harm him. He did not recognize the ward officer. He was given 0.5 gm. of sodium amytal intravenously, almost without effect, and an additional 0.5 gm was immediately given. This induced normal sleep. Six hours later he again became extremely restless and it was necessary to repeat the dose of sodium amytal intravenously, making a total of 1.5 gm in 6 hours. Within 4 hours the patient was again awake and was willing to stay in bed and take fluids and medication by mouth. He showed definite evidence of a paranoid psychosis, however, and believed that there was a plan in motion to do him bodily harm. It was impossible to reason with him on this subject, although in other matters he was moderately co-operative.

The conviction is general that action should be taken upon the basis of demonstrated need and as experience cumulates to indicate that such action is likely to attain ends in a nation comprising forty-eight states in which climatic, economic and social conditions vary greatly

this conservative setting the so-called "Principles and Proposals" were then set forth<sup>5-8</sup>

In the course of but seven years these principles and proposals have been generally accepted, and have already become almost ultraconservative — believe it or not — the committee was charged with revolution. Its members were accused of stabbing their fellow practitioners of American medicine in the back by releasing such radical material to the press. That the subject was the improvement of medical care and that the statement had been sent to the medical societies and medical journals of the country was generally overlooked. The fact that the editor of the *Journal of the American Medical Association*, prior to the date of release of the publication, referred to the statement as a revolt probably augmented the publicity. Amusing in retrospect is the fact that several members were severely criticized by the trustees and staffs of well known hospitals because of advocating the following:

That public funds should be available for medical research as essential for high standards of practice in both preventive and curative medicine, that public funds should be made available to hospitals that render service to the medically indigent and for laboratory and diagnostic and consultative services, and that in allocation of public funds existing private institutions should be utilized to the largest possible extent and that they may receive support so long as their service is in consonance with the above principles.

The advocacy of such proposals was felt to threaten the existence of private institutions. Well, many of these institutions are now seeking extensive financial support from the federal government, and, as remarked by Dr. Bauer, even the American Medical Association approves the allocation of public funds to private hospitals, as provided in the Hill-Burton Bill now before Congress. It is particularly amusing and informative to quote from an editorial that appeared at that time in the *Journal of the American Medical Association*<sup>9</sup>

It should not be necessary to point out again in the JOURNAL the danger of federal subsidies for medical schools. The danger of putting the government in the dominant position in relation to medical research is apparent. Still more serious is the fifth proposal, to the effect that the government subsidize private hospitals. The tender of governmental funds to such institutions appeals to the unthinking physicians who have endorsed these principles and proposals. Most conspicuous on the list are the names of those deans and heads of departments in medical schools who may have signed because they saw a possibility of getting government money for clinics and dispensaries. Certainly the unthinking endorsers of the principles owe to the medical profession some prompt disclaimers.

The recent hearings on the federal financing of medical research and education before the Senate Subcommittee on Wartime Health and Education<sup>10</sup> provide the best answer to such caustic comment. Indeed, under the leadership of essentially the same officials, the American Medical Association has

now proposed the establishment of a federal authority for medical research and education, with initial annual disbursements of \$25,000,000 for medical research and \$50,000,000 for medical education.\*

#### PROFESSIONAL LEADERSHIP

Perhaps the American Medical Association owes the medical profession some belated disclaimers. At least there are many physicians who believe that this lack of forethought on its part has inhibited the development of wise professional opinion concerning the precautions that should be taken in such expenditure of public funds, for there are, of course, obvious dangers to be avoided. Since such lack of leadership is of serious significance to the medical profession and the public alike, should we forget the past, agree with Dr. Bauer by saying, "So what?" and applaud the continuation of past policies in the present?<sup>†</sup> The American Medical Association still endorses the activities and emotional propaganda of the National Physicians' Committee for the Extension of Medical Service. Recent editorials in the *Journal of the American Medical Association* on the American Public Health Association's proposals for a nationwide health plan<sup>12-13</sup> and on the Health Conference's "Principles of a Nation-Wide Health Program"<sup>14-16</sup> still attest to a continuation of the same intolerant policy of suppressing constructive consideration of the problems confronting the medical profession. Possibly we, according to good democratic and conservative principles, should reflect on the wisdom of this leadership in order that we may intelligently vote as members of the profession to continue or discontinue it.

#### LIBERTY OF THOUGHT, SPEECH AND PRESS

Many physicians regret this tendency within the American Medical Association to restrict considered discussion and minority opinion, since they believe that it inhibits the development of sound progressive thought and is in no little degree responsible for the notoriously reactionary character of official medical opinion and policy. Certainly with few exceptions, such as the *New England Journal of Medicine*, the *Journal of the American Hospital Association*, *Hospitals* and the *American Journal of Public Health*, the record indicates that little opportunity is provided for the expression of minority opinion through the journals and other channels of so-called "organized medicine."<sup>‡</sup> Moreover, minority opinion within these medical societies is frequently buried by the practice of expressing the majority opinion as a unanimous one. A book en-

\*Recently the editor of the *Journal of the American Medical Association* appeared before a Senate committee and advocated the establishment of a national science foundation which would finance medical research and medical education.

<sup>†</sup>Witness the recent American Medical Association program.<sup>11</sup>

<sup>‡</sup>The *Journal of Pediatrics* has recently published interesting discussions in a section entitled "The Social Aspects of Medicine."



## SYMPOSIUM ON MEDICAL SOCIOLOGY

## MINORITY VIEWS ON IMPROVING MEDICAL CARE\*

ALLAN M BUTLER, M D †

LAST week Dr Bauer,<sup>1</sup> a trustee of the American Medical Association, spoke to you on that organization's view concerning the problems of medical care. The subject assigned me concerns views that differ from those of the American Medical Association. Strangely enough, in this democratic country, whose people believe in the free expression of minority opinion, the propriety of presenting such views on medical matters is questioned by some physicians. Hence, their mere consideration here will almost inevitably be subject to criticism. A politician would probably have declined the assignment. Indeed, an officer of the American Medical Association even refused an invitation to present to you the opinions of that body.<sup>2</sup>

To allay immediately either your fear or your expectation of radical opinion, let me assure you that I know of no one who does not heartily concur with the opinion expressed by Dr Bauer last week—namely, that extension or change of our medical services should be accomplished by evolutionary processes. No opinions expressed here, therefore, will be contrary to that sound conservative dictum. I trust, however, that we agree, that evolution connotes reaction manifested by a series of changes. From the standpoint of sociology, one may ask whether it is failure to react or reaction to changing circumstance that results in revolution rather than evolution. Was it, for example, reactionary monarchy or liberal philosophy that precipitated revolution in the evolution of representative government?

## EVOLUTION, NOT REVOLUTION

In considering a nationwide health program, it is pertinent to remember that, as stated by Terris,<sup>3</sup> compulsory health insurance, which is often considered to be an entirely new and unprecedented method of financing medical care in the United States, was used in this country as early as 1798. Much can be learned from study of the results of the act of Congress of that year, "for relief of sick or disabled seamen," which began by applying the method of monthly payroll deduction. Under this act grew the Marine hospitals. In 1884, Congress substituted a tonnage tax for the payroll-deduction method of financing the service, because the latter

put American shipping in an unfavorable competitive position. Perhaps there is food for thought here concerning the financing of individual state sickness-insurance plans by payroll deductions.

Over a course of years, the Marine Hospital Service evolved into the United States Public Health Service, which, as you know, is supported by general tax funds, and which, it may be pertinent to remark, maintains high administrative and scientific standards as well as freedom from political influence. The same high standards and freedom from political patronage or corruption pertain to the use of federal funds under the federal programs for crippled children and maternal and child health and for the Emergency Maternal and Infant-Care Program. With such evidence before us, need we accept the statement that funds expended under a nationwide health program must inevitably fall prey to the spoils system? A recent article in the *New England Journal of Medicine* by Wendell Berge,<sup>4</sup> Assistant Attorney General of the United States, provides reassuring comment pertinent to this question and to other aspects of medical sociology.

With all the experience of this and other countries with government sickness insurance and tax supported medicine, characterization of such medical-care programs as revolutionary reflects either historical ignorance or lack of awareness of current trends.

In 1937, as a contribution to the discussion of the subject of medical care in the United States, the Committee of Physicians for the Improvement of Medical Care formulated certain principles and proposals suggesting lines along which effort might be made by voluntary, local, state and federal agencies to improve medical care.<sup>5-7</sup> The introductory statement included the following:

It is recognized that the medical profession is only one of several groups to which "medical care" is of vital concern. Close co-operation between physicians, economists and sociologists is essential. Nevertheless the medical profession should initiate any proposed changes because physicians are the experts upon whom communities must depend. Unless the medical profession is ready to co-operate with these other groups they cannot expect to play successfully the part which they should play nor can they expect to enlist the sympathetic understanding of legislative bodies.

It seems to us probable that certain alterations in our present system of preventing illness and providing medical care may become necessary, indeed, certain changes have already occurred. Medical knowledge is increasing rapidly and is becoming more complex. Changes in economic and social conditions are taking place at home and abroad. Medicine must be mobile and not static if medical men are to act as the expert advisers of those who convert public opinion into action.

\*This is the eighth of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March 1945; they were sponsored by the Department of Preventive Medicine and were primarily intended for third year students. These articles will temporarily replace the reports "Medical Progress."

†Chief, Children's Medical Service, Massachusetts General Hospital; associate professor of pediatrics, Harvard Medical School.

que. That they should cherish the independence, freedom and artistic quality of their individual endeavor is natural and, in so far as it does not too greatly limit the quality and efficiency of their work, desirable. But the increase in medical knowledge, in the facilities necessary for its adequate application and in the cost of medical care render the average practitioner's position increasingly difficult and vulnerable. As so well outlined

Dr Dean Clark<sup>23</sup> in the second lecture of this series, the practitioner's income is meagre, his task and responsibilities immense, his independence more imaginary than real, and his future uncertain. He is therefore worried by, sometimes alarmed by and occasionally resentful of the change in the structure of medical practice that is slowly but surely occurring. His elected representatives, who are either salaried officials or elderly physicians successful under the present system, are usually the most ardent advocates of fee-for-service practice and bitterly defend its existence.

A hundred years ago the guilds in trying to protect their artisan interests resisted the integration of industry. Yet for better or for worse, integrated mechanized industry grew, the artisan was displaced, unemployment appeared, and wages fell. The industrial revolution came. Perhaps it is pertinent to ask. Can the American Medical Association in playing the guild role defend the physician artisan of today? Many think it a losing game. To find the American Medical Association on the defensive, as evidenced by Dr Bauer's lecture last week, and fighting only a delaying action against the progressive integration and prepayment of medical care is not so unexpected. It may, however, be puzzling to the young physician who has learned the medicine practiced by highly integrated group services, who aspires to contribute effectively to a high quality of medical service and to participate in the development and application of new knowledge and who has no vested interest in what may, not too inappropriately, be called the *status quo ante bellum*.

It is particularly pertinent that the young physician should consider the pattern of medical practice that will best serve society by quality and amount of service and thus better the public's respect for and financial support of the profession that will be his in the future. Will his experience with the inevitably defective emergency medical services of the armed forces make him an advocate of individualistic fee-for-service practice? Or will he, discounting the handicaps imposed by the emergency nature of these services, be impressed with the possibilities of well integrated group salaried practice? The considerations of a group of British physicians, as given in the *Medical Planning Research Interim General Report*,<sup>24</sup> set forth interesting opinion. The recent British White Paper provides more evidence concerning British trends. How irrelevant to current problems is the manner in

which representatives of the American Medical Association harp on the past defects of the English system, when those defects have been so generally recognized and are being corrected, and when no one is advocating the adoption of that system! Parenthetically, it may be remarked, that if the American Medical Association were correcting its past policies as constructively as are the British, mention of them would be irrelevant. Important questions about the English system are: Is it being discarded or extended? Do the doctors advocate its discontinuance? On the basis of past experience, how are they now proposing to extend government insurance? Instead of discussing these pertinent questions, spokesmen of the American Medical Association continue to comment on the English system of government sickness insurance in the manner that the Michigan State Medical Society<sup>25</sup> in 1934 declared was misrepresentation of fact and that representatives of the British medical profession have frequently described as inaccurate. Referring to comments made by the Bureau of Medical Economics of the American Medical Association, the secretary of the British Medical Association writes "Almost every page of the pamphlet provides matter for criticism on the score of inaccuracy or unfair presentation. [It] does not appear a very reliable account of the British Health Insurance system."<sup>26</sup> Another indictment of this bureau comes from an article by E. L. Brown,<sup>27</sup> research associate of the Russell Sage Foundation. "The potentially important Bureau of Economics," he writes, "which publishes statistics and studies of the distribution of physicians and forms of medical practice, is not only ultraconservative in philosophy, but the facts it presents are often incorrect or interpreted with bias, and even its statistical work is undistinguished."

The slogans and phrases resorted to by American Medical Association spokesmen are felt by many to favor an emotional rather than tolerant consideration and too frequently to constitute a misinterpretation that inhibits constructive thought. "It now becomes necessary," according to Dr Sensenich,<sup>28</sup> a trustee of the American Medical Association, "to protect the public by opposing the substitution of an unAmerican system of medicine with bureaucratic regimentation of patients and physicians, such as would destroy those American qualities of medical service that are most important to health and the American way of life." The National Physicians' Committee, which is supported in part by donations from pharmaceutical houses and whose activities have been endorsed by the House of Delegates of the American Medical Association, spends \$250,000 a year on such emotional propaganda, distributing dramatic pamphlets throughout the country through the agency of drugstores. Even a trustee of this committee, Dr Leland S. McKittrick,<sup>29</sup> characterizes its attack on the

titled *The Political Life of the American Medical Association*,<sup>17</sup> which should be read by all physicians, explains the manner of accomplishing this without openly transgressing the democratic principles of the Association. Is it or is it not odd that doctors, who are so generally individualists in character and practice, acquiesce in regimentation and suppression of minority opinion within their professional societies? Although most doctors are probably advocates of states' rights, they acquiesce in the American Medical Association's attempts to prevent state and other medical societies from expressing opinions different from its own.

For example, in June, 1934, the Board of Regents of the American College of Surgeons promulgated a prepayment plan for medical care at approved hospitals to members of the staffs of such hospitals and to physicians acceptable to such staffs. Immediately after this, the Judicial Council of the American Medical Association presented the following report,<sup>18</sup> which was unanimously adopted by the House of Delegates:

WHEREAS, the American Medical Association, including 100,000 physicians, is the only democratic body representing the organized profession of this country through delegates regularly elected through county and state medical societies, and

WHEREAS, other medical organizations and groups, representing selected groups of specialists, have from time to time issued pronouncements of policies in the field of medical economics and medical practice which do not represent the views of organized medicine and which purport to guide the medical profession and the public in the administration of medical affairs, and

WHEREAS, the House of Delegates of the American Medical Association has repeatedly condemned the issuing of such announcements and policies, and

WHEREAS, the Board of Regents of the American College of Surgeons, assembled in Chicago on Sunday, June 10, promulgated a policy including a prepayment plan for medical care restricted to so-called "approved hospitals," to members of the staffs of such hospitals and to physicians acceptable to such staffs, and

WHEREAS, this action of the Board of Regents of the American College of Surgeons has been spread to the people of the United States through the public press on the opening day of the annual session of this House of Delegates, therefore be it

RESOLVED, That the House of Delegates request the Board of Trustees of the American Medical Association and Judicial Council to ask the Board of Regents of the American College of Surgeons, who are themselves members of the American Medical Association, to explain the reasons for their action and to justify the attempt by this small group within a specialist organization to legislate for all the medical profession of this country, truly represented only by the American Medical Association.

Concerning the editorial in the *Journal of the American Medical Association* supporting this resolution, Dr J H Means<sup>19</sup> in a letter to the editor commented:

Your editorial entitled "Organized Medicine and Medical Care," July 14, 1934, is a truly amazing utterance. By it we learn that members of what you are pleased to call organized medicine are entitled to express no opinions on the great problem of medical service to the community, either as individuals or as minority groups, which differ from the official opinions of the House of Delegates of the American Medical Association. To say that [minority] groups are morally obligated to remain silent,

when their honest convictions run contrary to official doctrine, is hardly appropriate in a democracy like whose founders sought particularly to safeguard minority rights and opinions. I would like to quote from an editorial in the July 6 issue of the *Harvard Alumni Bulletin*: "Those who call for the preservation of American 'Institutions' do not always remember that among the most venerable and cherished of these institutions is liberty of thought and speech and press, and that nothing in America could be more 'radical' than its suppression."

The Board of Trustees of the American Medical Association replied, "It does not seem desirable to publish your communication addressed to the *Journal*."<sup>20</sup>

As stated in a paper read before the United States Chamber of Commerce,<sup>20, 21</sup> an extreme example of an attempt to suppress discussion and inhibit activities by physicians is furnished by the proposal in 1938 of the Council of the Medical Society of the State of New York to amend the bylaws as follows: "The component county medical societies, their officers, committeemen and members shall not initiate any policy, propose any legislation or participate in any activities that are contrary to the policies of the Medical Society of the State of New York." Fortunately, this was so objectionable to many members that the amendment was not accepted. Dr Bauer has taken exception to this reference because the proposal was overwhelmingly rejected at the meeting of the Council. I wonder, however, if he would not concede that discussion of the proposal prior to the meeting was significant. The recent publications of the Association of American Physicians and Surgeons and that association's advocacy of professional excommunication of physicians who do not subscribe to its policies attest to the fact that proposals of this nature do not altogether lack professional endorsement.

This matter of suppressing discussion within the profession is mentioned and briefly documented here not in the spirit of hostility, but rather to present the opinion of those who plead for a liberalism within the medical profession that will permit expression of minority opinions and thus tolerate consideration, reasoned debate and constructive criticism. Only by such democratic processes will the complicated problems of providing better medical care effectively be solved. Only by free discussion of current problems will evolution be orderly and revolution be avoided.

#### THE GUILD NATURE OF THE AMERICAN MEDICAL ASSOCIATION

That the American Medical Association should defend the present individualistic fee-for-service type of medical service is not surprising, as remarked by Dr Franz Goldmann in the discussion following his lecture<sup>22</sup> of several weeks ago. The great majority of its members are practicing and earning their living by that type of practice. These practitioners in some respects enjoy an independence that in our highly organized modern society is almost

h on the American Medical Association's attitude. If the medical profession would approach the problem with good will and eagerness for improvement, much could be accomplished. If, on the other hand, spokesmen of your profession belittle the need for improvement and display intolerance toward discussion, the evolution of beneficial change is inhibited. "A major obstacle," says a recent reviewer in *Fortune*,<sup>37</sup> "has been organized United States medicine, as represented by the century-old American Medical Association."

In a unanimous ruling concerning the suit brought by the Department of Justice against the American Medical Association and the District of Columbia Medical Society for restraint of trade, the Court of Appeals of the District of Columbia, through Justice Miller, made the following statement:<sup>38</sup>

Professions exist because the people believe they will be better served by licensing especially prepared experts to minister to their needs. The licensed monopolies which professions enjoy constitute in themselves, severe restraints upon competition. But they are restraints which depend upon capacity and training, not special privilege.

Neither do they justify concerted criminal action to prevent the people from developing new methods of serving their needs. There is sufficient historical evidence of professional inadequacy to justify occasional popular protests.

The better educated laity of today questions the adequacy of present-day medicine. Their challenge finds support from substantial portions of the medical profession itself. The people give the privilege of professional monopoly and the people may take it away.

The provision of a leadership that will defend the prestige and privilege of your profession by recognizing changing circumstance and directing constructive action depends in no small degree on you, young physicians.

#### INCREASING COSTS

As medicine has become more effective and the ultimate burden of illness to society has diminished, the cash costs of medical care have increased. As society has become more industrialized and individuals have become more dependent on wages, illness has with increasing frequency been associated not only with increasing costs but also with loss of wages and has therefore entailed greater financial stress. Thus, the inability of the sick to meet the costs of illness has increased. Families with incomes of \$3000 a year are reported by the American Medical Association to be unable to meet the costs of serious illness. Hospitals in large cities admit persons as charity patients whose family income is \$2500 a year. Physicians therefore today provide free service to many persons whose incomes are more than double the income of the average resident of the United States. Viewed from another aspect, our hospitals for chronic disease are used by persons whose productive abilities before affliction represented a cross-section sample of the community. Chronic illness in depriving them of their earning capacity, and subjecting them to the expenses of modern medical care has rendered rich and poor

alike unable to meet the continued costs of such illness. You or I, regardless of our present earning capacity, may, except by the grace of God, be the chronic invalid of tomorrow who will be a charity patient in a public institution. Thus, the charity tradition in medicine has extended far beyond its original concept. It now approximates a billion-dollar business that concerns a large portion of society. One may well ask: How fairly is the burden of this charity business dispersed? How adequately is it financed? How efficiently is it operated?

Although there is no doubt about the medical profession's carrying a great share of the burden, the degree to which this burden is distributed among doctors and the indirect recompense they receive for charity work is seldom considered in a business-like manner. The physician charges his private patients an arbitrary amount, according to a rough estimate of ability to pay, which will be adequate to compensate for the service rendered those who cannot or do not pay. This custom both accepts as satisfactory the meager information on which the arbitrary professional fees are based and ignores the totally inadequate means of distributing the amounts so collected among physicians according to the actual charity services rendered. Not infrequently the physician whose fees are highest contributes the least charity service. Too frequently the doctor whose patients can pay but small fees serves many without remuneration. Custom also results in the physician's giving medical care to the hospital's charity patients without remuneration in return for the prestige and experience so gained and for the privilege of utilizing hospital facilities for the care of his private patients. For the latter, however, the physician is hardly beholden to the hospital, because the latter, if reasonably well managed, makes a profit on the private patients whom the doctor provides. What happens to the hospital if the doctor provides no patient?

Thus, in these and possibly other respects the rationale of the current system of indirect professional remuneration for charity service is not too clear. But whatever the rationale, the amount of such service rendered by the profession attests not only to an awareness of its public-service role but also to its long-standing recognition of the inability of many persons to meet the costs of illness.

Great as these charity services and high as the standards are, they are but a fraction of what they might be. Indeed, there are those who believe that the unique persistence of the charity tradition is one of the principal impediments to a better quality of medicine. What is the evidence?

It has already been intimated that the charity tradition is the principal cause of the arbitrary character of professional charges. Can it be said with fairness that it has been intimately related to present inadequate financing of professional and hospital service alike and underpayment of labora-

Wagner-Murray-Dingell bill as "violent [and] somewhat undignified." The old bogie of a so-called "third party" coming between doctor and patient is again given a leading role. This cry concerning the evils of a third party and this charge that any modification of individualistic private practice will limit the "free choice of physician" have been used so loosely and misleadingly in regard to almost any well organized group health plan as to suggest either dishonesty or lack of intelligence. This propaganda does not mention that the excellent medical care provided by the Mayo Clinic, the Lahey Clinic, the Baker Memorial Unit of the Massachusetts General Hospital and all the larger university teaching hospitals throughout the country includes not the evil but the benefit of a third party. The propaganda does not mention that a majority of the American people have little free choice of physician in any significant sense. And such propaganda concerning the Wagner-Murray-Dingell National Health Bill<sup>29</sup> does not mention the fact that under this plan millions of people would be provided for the first time with the opportunity of choosing a family physician and that thus the American public would experience a greater free choice of physician than pertains today.

At a time when a recent survey made by the National Opinion Research Center of the University of Denver indicates that 68 per cent of representatively sampled Americans favor an extension of the Social Security Law to cover payments for doctor and hospital care, the distribution of distorted and hysterical propaganda may satisfy elderly physicians whose concern is to hang on to the *status quo* for a few years, but hardly contributes a sound solution to the public demand and your professional future. Are not your and the public's interests more effectively served by the careful analyses and constructive criticisms set forth in statements by the Committee of Physicians for the Improvement of Medical Care, Incorporated,<sup>30</sup> and by the Physicians' Forum,<sup>31</sup> and in the pamphlet covering the Health Program Conference?<sup>15</sup>

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and public health accomplish more now than it did then. By such comparisons, health programs were good in 1900 and perhaps even in 1850. A valid test is whether we do well and effectively about what we know how to do and can do. By this test there is no ground for complacency."

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The Maternal Mortality Committee of the Committee on Maternal Health of the Minnesota State Medical Association<sup>34</sup> makes the following statements in the summary of its report:

1 From July 1, 1941, through June 30, 1942, a review was made of the maternal mortality in the State of Minnesota.

2 The absence of any consultation in 56 per cent of the cases, the presence of less than 10 per cent adequate consultation, and the inadequacy of two thirds of the consultations which were obtained raises certain objections.

3 With a liberal interpretation, 43 patients (34 per cent) were well when first seen and died later.

4 One half of the inadequate consultations in our area were supplied by specialists, men who by training and experience should be capable of furnishing superior consultation.

5 There was an unfortunately high incidence of operative deliveries (56.2 per cent), some of the deaths resulting directly from the operative procedure.

6 Seventy-seven (82 per cent) had no pelvic measurement or less than the minimal requirements for adequate prenatal care laid down by the Committee for the Minnesota Maternal Study.

7 The great majority of physicians' office records were of very little value as regards accurate information, if indeed there were any records.

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10 The Committee agreed that 82 deaths (73 per cent) were preventable and that in all but 4 cases the physician was wholly or partially responsible.

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eneration of the young physician and the value his contribution to society appears not only to be unique but also to be dependent on the unique charity tradition of his profession

Proud as we may be of the generosity and idealism inculcated by this tradition in the past, one should not permit sentiment to obscure the incompatibilities between it and reality in the present. Much evidence indicates that the charity tradition not only imposes too heavy a burden on the profession but also provides a quality of medicine well below that which could readily be provided. The disruption of medical services by the war, the inevitable relocation of many medical veterans and the current discussion of a national health program make consideration of possible revisions of economic aspects of our system of medical care particularly opportune.

#### REDUCING THE BURDEN BY INSURANCE

At long last the public and the medical profession have come to realize that those who are unfortunate enough to suffer illness cannot be expected to pay the costs of modern medical care at the time when illness has decreased their income and increased their expenses. They appreciate that the liability is too extensive to be assigned to charity. They also see that post-payment bank-loan schemes of meeting the costs of illness merely provide more time to pay the costs that have fallen heavily on the unfortunate sick, whereas insurance or tax-supported services spread the costs to include those who have not suffered the financial burden of illness. Thus, schemes involving the latter methods of paying medical costs are being generally advocated. If wisely devised, there is little doubt that they will result in the more adequate financing of medical care. If they are unwisely devised, there will be little improvement in the financial support of better medicine and a wasteful expenditure of public funds on poor medical care.

The Committee on the Costs of Medical Care not only recognized this in 1930 but also recognized the important implication as regards the pattern of medical practice.<sup>38</sup> This committee, as you know, recommended that the budgeted medical service for home, office and hospital care be furnished largely by integrated professional groups, preferably organized around hospitals.

Representatives of the American Medical Association and of the state medical societies have belatedly admitted that application of the insurance cost-sharing principle to medical costs is per se neither economically unsound nor detrimental to the quality of medical care. But this admission merely introduces the problem. It neither contributes to the solution nor indicates the implication regarding the structure of medical practice that the Committee on the Costs of Medical Care recognized. Among the factors that deserve careful considera-

tion in any scheme is the establishment of proper administrative supervision and the development of well integrated units for providing medical care.

#### *The Problem of Administrative Supervision*

The payment of the costs of medical care by a third party — whether the government or a private agency — necessitates an administrative supervision of the cost and quality of the care provided that is not required when the cost is paid for by the recipient. When the transaction is between doctor and patient, there is a check on the amount of service requested and rendered, but when a third party pays for the service, there is no such check. The wide experience of commercial insurance schemes shows that 85 per cent of patients and doctors play fair, but that some 15 per cent run up costs that embarrass the schemes financially. Hence a mechanism for supervising the quality and quantity of care rendered is desirable. This, of course, cannot be provided without to some extent infringing on the almost complete independence that the individual practitioner thinks he enjoys today. The desire to maintain this pseudoindependence and to avoid being subjected to supervision is the main reason why the medical profession has opposed insurance medicine so long. Many physicians and medical associations, in a manner reminiscent of the old guilds, are defending this independence of the solo practitioner. Thus, as insurance medicine becomes inevitable, they are advocating forms of insurance medicine that are devoid of supervision.

Their first choice in defending this guild interest of practitioners is that payments under any government insurance scheme be made as cash benefits to patients, not as payments to doctors for service. This places a certain amount of money in the hands of the patient and leaves the doctor free to charge what he wishes. Obviously it is little more than a public dole under the pretext of being medical care. It makes no provision for economy in the expenditure of public funds nor does it reflect any concern for the quality of care purchased. Since this method of payment is usually recommended for governmental schemes and has rarely been advocated for any of the several schemes operated under the aegis of medical societies, the impracticability of such cash benefits is apparently fully appreciated but merely ignored in connection with government-insurance medicine.

The second choice of these defenders of the independence of physicians is that doctors be paid on a fee-for-service schedule by the insurance agency and be free to charge an additional fee to the patient. Under this scheme, for example, a doctor might be paid \$150 by the insurance agency for an appendectomy. The doctor then charges the patient an additional \$100, which nets him perhaps \$50 more than his regular private fee of \$200. Such a scheme ignores the equitableness of the total cost



tory and other hospital personnel? Or is it a primary factor in the lack of integration of hospital medical care and of student training?

With the exception of a few major teaching hospitals or private clinics, the service of doctors to hospital-ward patients lacks continuity. In the average hospital, the practitioners of the community care for the charity patients on a monthly rotation basis. One visiting physician may do the diagnostic workup of a case and start a well planned therapeutic regime that is disregarded or discarded by his successor. Or even if the planned therapy is continued, the doctor rarely has an opportunity to follow the therapeutic result intimately enough to provide maximal benefit to himself or his patient. Even if the patient returns to the outpatient department for follow-up, the chances are that he will be seen by a doctor other than the one who cared for him as a ward patient.

In the large teaching hospitals, the salaried staff may provide more continuity for ward care. But here also there is a lack of integration between outpatient and ward care. And here, too, the continued rotation or promotion of interns and residents through the various divisions of the hospital limits the continuity of the care they render.

Because physicians in the outpatient department provide their services on a voluntary basis for one to two and a half hours once or twice a week, continuity of service for the patient that needs care more than once or twice a week is almost impossible. If the examining physician wishes a consultation, he frequently cannot see the patient with the consultant because the consultant holds his outpatient clinic on another day. Thus, to no little degree, the charity aspect of hospital care limits the quality of such service, even though this may be good as compared to the average obtained from the private practitioner. Moreover, because it is an important factor in restricting hospital medical care to the ward and outpatient department, it limits the extent of the service rendered by integrated professional personnel and hospital facilities.

Quite rightly the physician feels that he is contributing enough charity service at the hospital. He therefore resents the extension of hospital service to the home lest it lead to one of two consequences, equally undesirable for him: that he be asked to see the patient at home who cannot afford to pay, or that the hospital through its resident staff provide home care to the patient who might otherwise pay a physician. Could there not be as clear a distinction between the paying and nonpaying patient at home as in the hospital? Resolution of the ambiguity would permit an extension of hospital services to include home care of the nonpaying patient. It would relieve the practicing doctor of the burden of home care of the nonpaying patient without infringing on his paying practice.

Such an extension would favor economy by lessen-

ing unnecessary hospitalization. For provision of home care by the hospital service would prevent not only unnecessary entry to hospitals but also undesirable prolongation of hospitalization. Second, it would improve medical education. The medical student during his four years and the intern and resident during an additional two to four years of hospital training rarely come in contact with a patient in his normal environment. Their basic patterns of medical thought about sick patients develop in the environment of hospital beds, operating rooms, laboratories and crowded outpatient clinics. Under these circumstances, it is difficult for the young physician to appreciate the particular stresses and strains in the daily life of his patient—economic burdens, family conflicts and mentally retarded children. He therefore forgets and forms the habit of belittling the effect of the patient's illness on his life and of his environment on his illness. Thus, the students' teaching tends to be limited to a therapy prescribed by medical science under the conditions pertaining in the hospital environment. These same limitations as regards personal and social implications apply equally to nursing education.

No wonder there is a demand for teaching psychosomatic medicine and more personal nursing care. But such emphasis will accomplish little. Students and teachers must be brought in contact with the patient's natural environment. The information it provides and its bearing on the health of the patient and the benefit of therapy should be utilized and appraised as thoroughly as are the data provided by the hospital laboratories. The solution of this problem of medical education is the extension of medical care from the hospital ward and outpatient service to the patient in his home.

The cost of medical education is also to some extent related to the charity tradition. As already mentioned, after his high-school education, three or four years of college and four years of medical school, the young doctor spends two to four years practicing his profession in a hospital. During this period he contributes from twelve to eighteen hours a day of service to his patients. On the assumption that the experience he thus obtains has a value that approximates that of the service he renders, he receives little or nothing the first two hospital years, perhaps \$500 the third year and possibly \$1000 a year for the fourth year. The students who can finance these many unremunerative years of medical education are not necessarily the best students or doctors. The system that provides such meager recompense therefore limits the selection of doctors. This undesirable limitation could be lessened if house-officer physicians were paid according to the value of the services they render. Surely the acquisition of valuable knowledge and experience in the early years of practice is not confined to the medical profession, yet the discrepancy between

self assure improvement in the financing of medical care

To some persons such a development of group service by hospitals and their staffs as indicated here may appear utopian. Let it be appreciated, however, that failure to provide for the development and utilization of such services under any extensive insurance scheme may destroy the very medical units from which the past improvement in medical care has emanated and on which future progress depends. Such being the case, it appears to be of concern to those interested in better medical care — doctors and laymen alike — to see that provision for the utilization and development of such services is included in any state or national health plan.

An orderly plan of financing and operating an efficient system of providing medical care should neither be damned as impractical nor hailed as the millennium. The resources made available by the one and the quality of care attained by the other will depend on a manifestation of the qualities that have brought medicine to its present high level. Lessening the occasion for charity and the limitations incident to it should provide a wider, not a narrower, field for the idealism that has under unfavorable circumstances sustained charity medicine in the past.

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to society and hardly distributes the cost of medical care satisfactorily. Moreover, it provides but little check on quality of care, other than that of gross abuse as detected by the accounting office.

### *The Development of Integrated Medical Services*

A potentially large insurance scheme that is now being organized recognizes the limitations of an insurance plan as regards economy and high quality where the service is rendered by individual physicians on a fee-for-service basis. This scheme, therefore, proposes to provide the medical service through groups of physicians-organized about hospitals. The success of the plan would appear to depend largely on two things. First, will the medical profession participate in the organization of such group services to be administered and integrated through executive committees of hospitals and their staffs? Second, will the public appreciate and accept the medical services of such groups rather than the services of individual physicians? The answer to the latter question will probably be "Yes." The answer to the former will depend largely on how extensively these organized groups of physicians can be made to include the majority of physicians in the area covered by the service. The problem involves the so-called "closed" or "open" aspect of hospital staffs. It seems clear that there will have to be well considered compromise between the two extremes of staffs closed to but a few doctors and open to all. However, if an adequate administrative or executive control body can be established for each hospital group, even teaching hospitals should be able to open their staffs appreciably without jeopardizing their standards or teaching functions.

The utilization of such group hospital units in the provision of medical care under medical-insurance schemes would provide certain definite advantages. Picture the potentialities of a community medical service emanating from the well integrated salaried staff and hospital facilities of the New York, the Presbyterian, the Bellevue, the Johns Hopkins, the New Haven or the Massachusetts General Hospital financed by insurance payments for the employed, government payments for the indigent and complementary voluntary contributions, the last being used primarily to foster advances and improvement in medical care. Reasonably sound calculations indicate that physicians' salaries of \$3000 to \$15,000 a year could be provided. The intermittent services of ward and outpatient physicians would be corrected. The lack of integration between inpatient and outpatient and home care would no longer be inevitable. The control of the functions of the co-operating physicians by the administrative committee would permit an opening of the staff without jeopardizing its standards. This extension of hospital staffs under controlled supervision would in

itself raise the quality of medical care in no little degree.

Such a development of group services about hospitals fits in with the Hill-Burton bill for extending and integrating hospital facilities. This proposed legislation would provide a type of service under a national health program, such as proposed by the Wagner-Murray-Dingell bill, that would limit many of the dangers inherent in governmental participation in the financing of medical care. It would maintain control of medical service at the local level by the existing units of medical service that have, under the present system, demonstrated their value in both medical education and medical practice.

Should teaching hospitals be properly incorporated into any such insurance scheme, they would receive an income for services rendered that should cover the cost of these services and thus alter the hospitals' character as charity institutions. Since no medicine is more expensive than cheap medicine, it is essential that this income be sufficient to cover adequately the costs of both hospital and professional services. A clear distinction between these two categories of service and the allocation of specified charges for payment of physicians seems highly desirable to avoid exploitation of physicians by institutions. The result of inclusion of house-officer services among the professional services to be remunerated would be that young interns and residents would receive more adequate salaries than pertain today and that the cost of medical education would thus be reduced. Further elimination of the present financial barrier to entering the medical profession might be accomplished by provision of federal loans to needy students on a simple, businesslike basis. The loan would be granted to qualified applicants on the basis of repayment by working in government hospitals or other medical services. Such a logical stipulation would prevent abuse of the privilege. The Government's risk would be little, and benefit would be great. The services of these physicians in governmental institutions would improve the quality of their staffs and make their conversion to teaching institutions possible. Should this occur, improvement in the quality of service would follow almost axiomatically. Such a financing of medical education would benefit society and student alike.

The adequate financing of research and of medical education in general deserves, of course, a consideration that will remove both of these from a precarious dependence on philanthropy.

Whether the major portion of the funds collected under insurance plans be the result of voluntary association or of legislation, the responsibility placed on the administrative agencies for their wise disbursement should be stressed. An increase in the collection of funds for medical needs does not in

itself assure improvement in the financing of medical care.

To some persons such a development of group service by hospitals and their staffs as indicated here may appear utopian. Let it be appreciated, however, that failure to provide for the development and utilization of such services under any extensive insurance scheme may destroy the very medical units from which the past improvement in medical care has emanated and on which future progress depends. Such being the case, it appears to be of concern to those interested in better medical care — doctors and laymen alike — to see that provision for the utilization and development of such services is included in any state or national health plan.

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32081

#### PRESENTATION OF CASE

A seventy-three-year-old man was admitted to the hospital in an unconscious state

According to his wife he had been in good health except for hypertension of about ten years' duration. Ten months before admission he had a "stroke," with paralysis of the left side of the face followed by partial recovery. One and a half hours before admission he returned home from a walk and collapsed, being found unconscious.

Physical examination revealed a slightly cyanotic, restless man with cold hands and feet. The pupils were small and equal. The eyegrounds were not remarkable. The right elbow was stiff. The left leg was smaller than the right. The cardiac rhythm was irregular, with an apical systolic murmur. The lungs were clear. The liver was questionably enlarged. The right knee jerk was more active than the left. The Babinski sign was absent on both sides.

The temperature was 98°F, the pulse 150, and the respirations 30. The blood pressure was 110 systolic, 65 diastolic.

The white-cell count was 16,500. The urine contained no sugar. An electrocardiogram revealed auricular fibrillation, with a rate of 90, and evidence of left-axis deviation. ST<sub>1</sub> and ST<sub>2</sub> were depressed, as were ST<sub>4</sub> and ST<sub>5</sub>, T<sub>1</sub>, T<sub>2</sub>, T<sub>3</sub>, and the T wave in CF<sub>2</sub> were upright, the T wave in CF<sub>4</sub> and CF<sub>5</sub> was diphasic.

The patient remained unconscious, cyanotic and dyspneic. Two hours after admission he was given oxygen, as well as 3 cc of Cedilanid intravenously. The respirations became somewhat more regular, but the patient became restless and violent. Three cubic centimeters of paraldehyde was administered. The blood pressure fell to 80 systolic, 40 diastolic. The cyanosis increased. A unit of plasma was given intravenously. The heart sounds became distant, and the respirations assumed a Cheyne-Stokes character. After a short episode of tachycardia the patient expired, three hours after admission.

## DIFFERENTIAL DIAGNOSIS

DR ALAN R MORITZ\* In a conference of this kind it is unusual to have a pathologist make the ante-mortem diagnosis. His position is generally a little more secure than mine is at the moment.

When an apparently healthy seventy-three-year-old man has an unexpected syncopal attack and dies shortly thereafter without regaining consciousness, the cause is usually found to be either a cerebral vascular accident or an acute coronary insufficiency. Am I correct in assuming that there was no reason to suspect that head injury had anything to do either with his collapse or with his subsequent death? When and where did he collapse and did anyone see him fall?

DR GEORGE C COTZIAS He was at home and apparently was found lying on the bathroom floor.

DR MORITZ How long had he been unconscious before he was found?

DR COTZIAS No one knew how long he had been there, although they thought that it was probably less than half an hour.

DR MORITZ The reason I ask where the patient was found is that it is not particularly unusual for a person to strike his head when he falls as a result of a syncopal attack. Even though he may not have sustained a visible injury to the skull, subdural bleeding, sometimes bilateral, is often found at autopsy. I cannot be sure that that did not happen to this patient, but if it did, I regard it as an incident to the affair and not serious.

I am discarding cerebral apoplexy. I should be surprised if this man had collapsed and died as a result of intracerebral hemorrhage without sufficient clinical evidence to have at least warranted a lumbar puncture. I am reading between the lines a little bit in passing over this cerebral hemorrhage as I have, and I may not be justified in so doing. If I am wrong, my fault is in having too much confidence in the house officers. It does not appear that the patient manifested any signs or symptoms of cerebral disturbance that could not have been accounted for on a basis of circulatory failure. According to my clinical colleagues the electrocardiographic changes indicate coronary insufficiency. Am I correct in believing that there was no history suggestive of previous anginal attacks?

DR COTZIAS The history gave no evidence of angina.

DR MORITZ It is not at all uncommon for persons who have never complained of angina to die unexpectedly of coronary disease. Does the protracted period of unconsciousness that this man had between his initial seizure and his death detract from the diagnosis of acute coronary insufficiency? Considering his age I do not believe that it does. It is true that a young or middle-aged man is likely to die very quickly after the onset of an attack of coronary insufficiency of sufficient severity to cause

\*Professor of legal medicine, Harvard Medical School

syncope It is not infrequent, however, for older men to survive such episodes of coronary insufficiency Perhaps the presence of cerebral arteriosclerosis predisposes to loss of consciousness following a relatively small impairment of the systemic circulation

I am somewhat disturbed at the extreme restlessness of this patient His agitation was of such duration and violence as to require paraldehyde sedation Although I know of no incompatibility between restless unconsciousness and the kind of cerebral anoxia that might result from coronary insufficiency, I must confess that I have never personally encountered so protracted a period of motor stimulation due to central circulatory failure Of course brief agonal convulsive seizures frequently precede death from coronary disease, and restless unconsciousness or convulsions are often reported in the Stokes-Adams syndrome I am willing then with some misgiving to accept the restlessness as an unusual but nevertheless plausible complication of circulatory failure caused by coronary insufficiency

To me the leukocytosis is best explained as a reaction to a myocardial infarct that was probably present for some hours before the occurrence of the terminal syncopal attack It appears that this recent infarct was at first asymptomatic Perhaps his collapse and death were due to tamponade caused by rupture of the heart at the site of a recent and previously asymptomatic infarct

DR. BENJAMIN CASTLEMAN Are there any further comments?

DR. PAUL D. WHITE The electrocardiogram is somewhat equivocal It is not normal It may indicate some disturbance in the circulation to the posterior wall of the left ventricle, but it is not typical of a posterior myocardial infarction There is no elevation of the ST segments in Leads 2 and 3, although there is considerable ST depression in Leads CF<sub>1</sub> and CF<sub>2</sub>

DR. MORITZ I recognize that my clinical colleagues were at a disadvantage in expressing an opinion based on a description rather than on an examination of the electrocardiograms themselves

DR. WHITE They would not have been able to do much more had they seen the films The left-axis deviation could have gone with a hypertensive pattern, with the fibrillation due to cardiac irritability

DR. CHESTER M. JONES I should like to raise the question of the advisability of giving plasma in a patient with beginning cardiac failure It seems to me an unwise move The mere fact that the blood pressure fell is no indication for the administration of plasma in a case of this sort

DR. COTZIAS We believed that the picture of shock was more pronounced than the picture of heart failure

DR. WHITE We have often raised that question, whether patients with acute coronary occlusion in

shock may be helped by plasma We do not know

DR. JONES It is an important therapeutic decision to make in a case like this in which some harm might ensue

DR. WHITE It is conceivable that it might help if the myocardium has sufficient reserve

#### CLINICAL DIAGNOSIS

Myocardial infarction?

Cerebrovascular accident?

#### DR. MORITZ'S DIAGNOSES

Coronary thrombosis

Myocardial infarct

Rupture of myocardial infarct, with cardiac tamponade?

#### ANATOMICAL DIAGNOSES

Media necrosis aortica cystica, with rupture of aorta into pericardium.

Cardiac tamponade

#### PATHOLOGICAL DISCUSSION

DR. CASTLEMAN At autopsy the pericardium was filled with a liter of fresh unclotted blood It arose not from a tear of the myocardium, but from one of the ascending aorta The aortic lesion was not a dissecting aneurysm, however, but a complete through-and-through tear of an aorta that had the severest media necrosis cystica that we have ever seen It is the first case that we have had where the external rupture occurred simultaneously with the intimal tear, so that there was no chance for dissection

DR. WHITE There might have been some occluding pressure from the blood around the right coronary artery, which would explain the electrocardiographic changes

Where was the point of rupture?

DR. CASTLEMAN In the ascending aorta, about 1.5 cm above the valve

DR. WHITE Did slow bleeding occur before hemorrhage took place into the pericardium?

DR. CASTLEMAN I do not believe that the patient could have gone into syncope unless he had had a lot of bleeding at first If it were a slow leak, he probably would not have fallen He must have had a large rupture at the start and lived for four and a half hours

DR. WHITE Do you think that it all might have been due to tamponade?

DR. CASTLEMAN Yes, but he must have had a major break at the start to cause him to faint We have had a few patients with syphilitic aneurysms who have lived for some time after symptoms of rupture What is the sequence of events in your experience with ruptured aneurysm, Dr. Moritz? Do such patients often have a hiatus before they die?

DR. MORITZ We have had two or three who have I am surprised in this case that the man bled enough

into the pericardial sac to lose consciousness and yet was able to survive for three or four hours

DR WHITE Did he bleed in both directions along the aorta?

DR CASTLEMAN All along the adventitia of the aorta and the pulmonary artery The hemorrhage even extended along the adventitial coats of the smaller pulmonary arteries into the lung, a condition that we have seen before in patients with ruptured aortas

## CASE 32082

### PRESENTATION OF CASE

A forty-four-year-old Irish truck driver was admitted to the hospital complaining of shortness of breath, orthopnea and edema of the legs

Four years before admission he had been rejected by his draft board because of "heart disease" He remained symptomless, however, until fourteen months before admission, when he complained of weakness and fell while working Although he stopped work, he noticed, five months later, that he was gradually losing weight He developed anorexia, vomiting, abdominal pain, dyspnea and orthopnea He was digitalized and his symptoms subsided He was easily fatigued and had anterior chest pain on exertion Four months before admission he discontinued digitalis and resumed full-time work Soon, however, without any preceding trauma, infection or undue exertion, he noticed the sudden onset of extreme shortness of breath He also complained of pain in the anterior chest Two months later he again consulted his physician, who gave him more digitalis Three weeks before admission he was confined to bed, and two weeks later he entered another hospital, where he received digitalis and ammonium chloride After leaving the hospital of his own volition, he began to cough up small amounts of thin, bloody sputum, and swelling of the legs progressed rapidly For the two days before admission he had passed no urine

The past history revealed no evidence of rheumatic fever or venereal disease

Physical examination revealed a well developed and nourished man who was dyspneic, orthopneic and cyanotic He did not complain of pain Severe arteriosclerosis was apparent The fingers were clubbed The pupils were normal The neck veins were pulsating The heart was enlarged to the right and to the left, the left border being 12 cm from the midline in the fifth intercostal space The point of maximal impulse was in the anterior axillary line at the sixth interspace, with a forceful thrust A-Grade III diastolic murmur and a Grade I systolic murmur were heard at the apex, and both were transmitted to the axilla A Grade II diastolic murmur and a Grade I systolic murmur were heard over the aortic area The latter was transmitted to the

neck The aortic second sound was obliterated A diastolic thrill was palpable in the suprasternal notch The left lung was clear At the right base, fremitus was absent, breath sounds were diminished, and crackling inspiratory rales were heard, percussion revealed flatness over this area The abdomen apparently contained no fluid The liver edge was palpable four fingerbreadths below the right costal margin, it was firm, sharp, slightly tender and not pulsating The spleen was not felt The lower extremities showed marked pitting edema, which extended to the hips

The temperature was 97°F, the pulse 80, regular and full, and the respirations 20 The blood pressure was 115 systolic, 75 diastolic

The red-cell count was 4,900,000, with 14.6 gm of hemoglobin The white-cell count was 11,700 The urine was clear and acid, with a specific gravity of 1.017 It gave a +++ test for albumin, and the sediment contained 25 white cells, no red cells and many granular and hyaline casts per high-power field The nonprotein nitrogen was 31 mg per 100 cc, the total serum protein 5.2 gm, and the prothrombin time 30 seconds (normal, 18-20 seconds) A blood culture was negative

An x-ray film of the chest on admission revealed that the heart was large, especially in the region of the left ventricle, which was extended downward and laterally The cardiothoracic ratio was approximately 20/29.8 The left auricle was enlarged There were areas of calcification in the region of the mitral and aortic valves The hilar and pulmonary vessels were diffusely engorged, and both lungs were hazy There was a small amount of fluid in both pleural cavities There was a localized area of increased density in the right costophrenic sinus, which in the lateral view was seen to be round A similar area was seen somewhat higher in the right lower lobe in close contact with the interlobar septum

Three days after admission, the patient's edema had markedly subsided but the temperature continued to rise, reaching as high as 102°F Hemoptysis continued, and the liver remained enlarged The fluid in the right pleural cavity increased A friction rub was heard for a short time in the right axilla and then disappeared

Another chest film taken on the sixth hospital day showed hazy homogeneous density occupying the lower half of the right lung field and obscuring the outline of the diaphragm and heart Jaundice appeared on the eighth hospital day On the ninth hospital day, 1100 cc of bloody fluid was removed from the right pleural cavity It had a specific gravity of 1.012, with 37,000 red cells and 1700 white cells per cubic millimeter, 44 per cent of the latter being polymorphonuclear cells and 56 per cent lymphocytes The following day, after a period of fluttering, irregular heart action, the patient expired

## DIFFERENTIAL DIAGNOSIS

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find any microscopic evidence of rheumatic infection in the myocardium. On the other hand, I realize that I am a prejudiced party on this issue. I can rarely find microscopic evidence of rheumatic involvement in a case of calcareous aortic stenosis, whereas other pathologists find it quite often.

DR CHARLES S. KUBIK: Did you find a source for the emboli?

DR MALLORY: There were numerous thrombi in

the leg veins. The larger veins were free, but when we cut into the muscles of the calf, the intramuscular vessels were thrombosed and there was some degree of myositis of these calf muscles as well. I personally think that the onset of jaundice was connected with the pulmonary infarction. Any great degree of jaundice is unusual with simple congestive failure, but with the onset of pulmonary infarction it becomes almost the rule rather than the exception.

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COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## RATION'S END?

WE ARE being prepared, at the time of this writing, for the abandonment of sugar rationing at some time in the not too distant future, and with it the ending of the entire food rationing program. This does not necessarily indicate an abundance of sugar on the way, any more than the removal of restrictions on other foods has been followed by a surfeit of the market with them, — butter and margarine are currently not to be found in the local stores, — nor does it mean that we shall be living hereafter in a land of corn and wine, whatever definition may be given to the former word in this particular. It does mean that soon a Cuban and later a Philippine crop of sugar will place this article of food in the ranks of others supposed to be reasonably plentiful, and the

members of medical advisory committees may end their tasks with heads unbowed, if bloody.

Sugar, as a rationed commodity, has rarely been found by the Medical Advisory Committee to the Regional Office of Price Administration to be required in larger quantities than those allowed by basic rationing. Other sugars and other forms of carbohydrate have been too easily available, and there are few diseases, if any, that require cane sugar in their treatment. It is therefore at least of interest to note the numbers of persons uncovered since local rationing boards went out of existence who have been receiving extra allotments of sugar, apparently without benefit of approval by any medical advisory committee. In fact, a recent report from the Regional Office of Price Administration since the files from the state have been consolidated, indicates that more than 2000 persons in Massachusetts have regularly been receiving extra sugar since 1942, of which number only a very small fraction had ever had their requests reviewed, as required by regulation, by a medical advisory committee. No one had realized how much sweetness was being wasted on the desert air!

Two thousand out of a population of 4,316,721 is no great matter, and we might, indeed, consider with amazement the fact that so few have owed so little to so many. In our sturdy democracy, however, where each rationing board might well have sought to be a law unto itself, we now wonder, idly, how many other importunate persons may have owed their teeming fleshpots to a local handout.

## WAIVER OF DISABILITY

ATTENTION is called to a letter published elsewhere in this issue of the *Journal* in which the commanding officer of an overseas station hospital clarifies a misunderstanding concerning the so-called "waiver of disability" on the part of an officer entering the armed services of the United States. There can be no doubt that it is generally believed that, if a man or woman accepts a commission in the Armed Services and at the same time has a physical defect that can serve as a source of future trouble, he expects, as part of the sacrifice he must make for his country, to "sign a waiver," which will

release the Government from all responsibility for the care of conditions subsequently arising out of the disability that has been waived

Such a belief seems to be entirely wrong. If the author of the letter is correct, — and there is no reason to suppose that he is not, — this false belief is based on an equally erroneous misconception. It is the Government that does the "waiving." By so doing it does not deprive the physically defective officer of his right to obtain redress for disablement arising in the line of duty even though it may be secondary to his disability. Instead, the Government assumes the risk and "accepts the person in spite of the defect."

This is an important point, and one that should be drawn to the attention of all veterans. From conversations heard here and there it is apparent that there are a considerable number of disabled veterans who think that they are not entitled to apply for benefits from the Government because they waived their rights to make such application when they entered the service. Veterans' organizations should publicize this mistake so that it can be corrected at once. Such veterans should be no longer deprived of the help that they may need badly and are certainly entitled to.

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

**MULLIGAN** — Francis J. Mulligan, M.D., of Newton, died February 5. He was in his forty-fifth year. Dr. Mulligan received his degree from Boston University School of Medicine in 1928. He was Newton school physician and a member of the staff of the Newton-Wellesley Hospital. His widow, four sisters and a brother survive.

**STEVENS** — Harry L. Stevens, M.D., of New Bedford, died January 29. He was in his seventy-sixth year. Dr. Stevens received his degree from Baltimore Medical College in 1891. He was formerly physician to the overseer of the poor and city physician. In 1936 he was appointed to a seven-year term on the State Board of Registration in Medicine.

**TIMMINS** — Edward F. Timmins, M.D., of South Boston, died December 11. He was in his sixty-fifth year.

Dr. Timmins received his degree from Harvard Medical School in 1904. He served for many years as medical inspector of the South Boston district and supervising physician for the Boston School Department. He was a member of the South Boston Medical Club, of which he had been president. He became a fellow of the Massachusetts Medical Society in 1911 and first served as councilor in 1936; he was subsequently appointed to the Committee to Study the Practice of Medicine by Unregistered Persons and was elected a censor by his district society in 1944.

His widow, two sons and two daughters survive.

## MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

**George L. Schadt, Chairman**  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

**WOODWARD** — Samuel B. Woodward, M.D., of Worcester, died January 29. He was in his ninety-third year.

Dr. Woodward received his degree from Harvard Medical School in 1878. He spent more than two years studying abroad. For many years he was consulting and visiting surgeon at St. Vincent and Worcester City hospitals. He was a trustee of Worcester State Hospital and chairman of its board of trustees. He was a former president of the Massachusetts Medical Society and also of the Alumni Association of Boston City Hospital. He was a fellow of the American Medical Association and of the American Academy for the Advancement of Science. He retired in 1921 after forty years of practice.

## NEW HAMPSHIRE MEDICAL SOCIETY

**SCOTT** — Nathaniel H. Scott, M.D., of Wolfeboro, died January 25. He was in his ninety-fifth year.

Dr. Scott received his degree from Bowdoin Medical School, Maine, in 1874. He had practiced general medicine and surgery in Wolfeboro from 1880 until his retirement about twenty years ago.

His widow, a son and five daughters survive.

## MISCELLANY

### DEPARTMENT OF ANESTHESIA AT MCGILL

The Department of Anesthesia has recently been created at McGill University, according to Dr. Wesley Browne, chairman of the department. Its stated objectives are as follows: to improve the teaching of anesthesia to the undergraduate student in medicine, to enhance the opportunities for learning anesthesia by the interns of the hospitals connected with the University, to maintain a three-year diploma course in anesthesia for those graduates in medicine who desire to become specialists, and to develop investigation in anesthesia, both within the department, correlating the clinic and the laboratory, and in co-operation with other departments of the University.

### AMERICAN BOARD OF OPHTHALMOLOGY

In regard to the substitution of a preceptorship for residency in an ophthalmic hospital, Dr. S. Judd Beach, secretary of the American Board of Ophthalmology states that the Board has always accepted such training in favorable cases. It should, however, be pointed out that neither a residency nor a preceptorship suffices in itself to meet the requirements of the Board. Each case will still be judged on its merits in accordance with the Board's standards.

In entering on a preceptorship, certain conditions should be kept in mind. First the student will profit most after a sound course in the basic sciences of the eye and of vision, such as optics, physiology, pathology, bacteriology, chemistry, pharmacology, anatomy, embryology and neurology, and in the relation of the eye to general disease. This is essential for a residency, more so for a preceptorship.

Although men have been accepted from preceptors not diplomates of the Board, it is obvious that the Board has more information about those teachers who have passed its examinations. Any preceptor should understand that he is assuming a responsibility in taking a student and is not merely obtaining help in the drudgery of his office. He should be willing to give time to clinical training and the use of apparatus, such as the slit-lamp, ophthalmoscope and tonometer, and to directing the student's practice in surgery on animal eyes, assisting in operations and ultimately in the performance of them.

To cover the same amount of ground will take much longer in a preceptorship than in a residency, and students should accept opportunities to take hospital positions of all sorts as they become available.

## CORRESPONDENCE

### WAIVER OF DISABILITY AND THE ARMY'S NEED FOR SENIOR MEDICAL OFFICERS

To the Editor: Reference is made to the letter "An Appeal," signed by W. A. R. Chapin, that appeared in the October 4, 1945, issue of the *Journal*. In this letter I note the statement that the medical officer in question "waived a disability." This is an error that is widespread and should be corrected.

For nearly three years I was on the staff of the surgeon of one of the nine service commands in the Continental United States, during which time I was the sole arbiter of who was or was not physically qualified for military service. This period covered the expansion of the armed forces, which began in September, 1940. I therefore speak with a detailed and accurate knowledge of the factors involved.

No officer ever waived or signed a waiver of his physical defects. Late in 1941, for reasons not clear to me, the War Department adopted certain policies in the case of officers who had defects that technically disqualified for military service. Briefly stated the policy was to require an officer who was found to have certain defects to sign a certificate admitting the presence of the defect and requesting that the defect be waived for the purpose of entering on active duty. If the reviewing authority decided that the defect did not constitute a bad military risk he (the reviewing authority) accepted the officer for general or limited military service and waived the defect for the Government. The subject officer waived nothing!

One cannot legally waive a defect that he or she may have. There are Supreme Court decisions on this, which may be briefly summarized as follows: The right to compensation is a statutory right and as such cannot be waived by a person as a condition of employment by or service in the armed forces. In other words, a defect existing prior to entry into the service, which becomes aggravated to a disabling degree by reason of service in the armed forces, is compensable just as though the defect were incurred by reason of such service. Thus, by waiving the defect, or more correctly, by accepting the person in spite of the defect, the Government assumes the risk.

I shall not attempt to pass judgment on the complaint offered by the officer who wrote the letter, but I must speak in defense of the Army. I believe that I am qualified, since I have been in command of a large hospital out here for almost two years.

In the mad rush to get physicians out of the Army the hospitals in the Pacific are being stripped of competent professional personnel. Transfer of medical officers with high-point scores removes the most competent ones. The low-point men who remain are, almost without exception, rather recent graduates with no qualifications in any specialty. As matters now stand, I shall lose my chiefs of medicine and surgery in January, and so far as I now know, they will of necessity have to be replaced by young men who have no special qualifications for such vitally responsible positions. What recognized civilian hospital would accept as a consultant in surgery a physician who had graduated in 1942, had served a nine-month internship and had then acted as a

ward surgeon or assistant for two years? The answer is obvious, but that is exactly the situation we are now confronted with out here. The consequences may well result in a Congressional investigation that could not fail to reflect unpleasantly on the profession.

This station hospital is now part of the permanent garrison on an island that is (or was) an integral part of the Japanese Empire. I am not a Regular Army officer but an old reservist from the last war who has been on active duty for more than five years and who has volunteered to remain out here until April 1, 1946, in an effort to reorganize this hospital with such personnel as is available. I have had an almost complete turnover of personnel since V-J Day, and within the next six weeks I shall be the only person left in this organization who was in it at that time. Most of the personnel are "fresh out from the States."

There are two sides to every question. This matter is particularly difficult, especially for those of us in command positions.

COLONEL \_\_\_\_\_, M.C., A.U.S.  
Commanding

## NOTICES

### ANNOUNCEMENTS

Dr. F. Dennette Adams has returned from military service and resumed the practice of internal medicine at 226 Marlborough Street, Boston 16.

Dr. Robert H. Barker, having returned from service in the United States Navy, is resuming the practice of obstetrics and gynecology at 330 Dartmouth Street, Boston.

Dr. Martin A. Berezin, having returned from active service with the United States Army Medical Corps, announces the opening of his office at 117 Bay State Road, Boston, for the practice of psychiatry and neurology.

Dr. J. Charles Drooker, having recently completed military service in the United States Army, is resuming the practice of diseases of the ear, nose and throat at Hotel Gralyn, 20 Charlesgate West, Boston.

Dr. Robert H. Goodwin, having returned from active duty in the United States Navy, is resuming the practice of obstetrics and gynecology at 15 South 6th Street, New Bedford.

Dr. Ward I. Gregg announces his return from military service and the reopening of his office for the practice of gynecology and surgery at 266 Beacon Street, Boston.

Dr. Thomas M. Hearne, having been released from active duty with the United States Navy, announces the reopening of his office at 43 Stratford Road, Melrose, for the practice of medicine and obstetrics.

Dr. I. H. Jaffee, having returned from active service with the United States Army, announces the opening of his office at 483 Beacon Street, Boston, for the practice of allergy.

Dr. Allen S. Johnson announces his return from service with the United States Navy and the opening of an office at 276 Bridge Street, Springfield.

Dr. James J. Regan has resumed the practice of ophthalmology at 520 Commonwealth Avenue, Boston.

Dr. Henry R. Viets announces the removal of his office from 262 Beacon Street to 20 Gloucester Street, Boston.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 28

FRIDAY, MARCH 1  
\*10:00 a.m.-12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.  
10:50 a.m. Systemic Therapy of Skin Conditions. Dr. George E. Morris. (Postgraduate Clinic in Dermatology and Syphilology) Amphitheater, Dowling Building, Boston City Hospital.

MONDAY, MARCH 4  
\*12:00 m.-1:00 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital.

(Notices continued on page xxi)

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## MEDICAL SHOCK. ABNORMAL BIOCHEMICAL CHANGES IN PATIENTS WITH SEVERE, ACUTE MEDICAL ILLNESSES, WITH AND WITHOUT PERIPHERAL VASCULAR FAILURE\*

CHARLES S. DAVIDSON, M.D.,† JESSICA H. LEWIS, M.D.,‡ HENRY J. TAGNON, M.D.,§

MARGARET A. ADAMS, A.B.,¶ AND F. H. L. TAYLOR, Ph.D.||

BOSTON

RECENT studies in the so-called "shock syndrome" in animals have definitely associated this syndrome with certain biochemical abnormalities.<sup>1,2</sup> Hyperglycemia, lactic acidemia, lowered alkaline reserve and changes in the partition of the nonprotein nitrogen of the blood plasma have been reported in this condition. In hemorrhagic shock, increases in the plasma alpha amino nitrogen have recently been reported.<sup>3,4</sup> Anoxia has been a frequent finding in shocked animals, and furthermore, anoxic anoxia itself has been found to produce some of the biochemical changes attributed to shock.

Recent reports from this laboratory have shown that in man marked biochemical changes of a similar nature to those reported in animals occur following thermal burns.<sup>5,6</sup> Such changes were found to be significantly associated with the severity of the thermal injury and the presence of shock. Aub<sup>7</sup> has reported abnormalities of carbohydrate metabolism following trauma.

The present investigation was undertaken to study the relation of peripheral vascular failure, uncomplicated by traumatic conditions, to the biochemical changes previously reported in shocked animals and following injury in man. The subjects used were patients suffering from severe medical illnesses, with or without the presence of peripheral vascular failure. In all cases there was no indication in the history that clinical diabetes was present.

### METHODS

Twelve patients suffering from severe illnesses were studied. Their ages ranged from nineteen to eighty, 9 patients being over fifty years of age. There were 7 males and 5 females. No patient gave a history or had clinical evidence of diabetes mellitus. Five patients were admitted with severe infections, 4 with severe cardiovascular involvement, 1 of whom suffered from pneumococcus (Type 1) pericarditis, 2 following the ingestion of poison, probably an overdose of a barbiturate, and 1 with a massive gastric hemorrhage. Ten patients had some degree of peripheral vascular failure, the degree being estimated independently by two physicians. The criteria used in estimating the degree of failure are shown in Table 1. The essential details of the cases studied are given in Table 2. The patients were treated by specific or symptomatic therapy in accordance with the requirements of their clinical condition. Where such therapy had a bearing on the biochemical changes encountered it is commented on in the appropriate place in the text. Autopsies were obtained on certain patients who died, and the significant findings are stated in the text.

Blood and urine samples were obtained during and following the period of circulatory failure and analyzed for glucose (Somogyi-Benedict method), lactic acid, carbon dioxide content or combining power, alpha amino nitrogen (ninhydrin method) and oxygen. Tolerance for glucose was frequently determined by the intravenous method.<sup>8</sup> Prothrombin times, icterus indices and hemoglobin levels were determined. The methods used for the various determinations have been stated elsewhere.<sup>6</sup>

### RESULTS

The over-all data are presented in Table 3. They are arranged in order of decreasing lactic acid concentration in the blood plasma or serum. To arrive at the designation of the degree of peripheral

\*From the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard) Boston City Hospital and the Department of Medicine, Harvard Medical School.

†The work described in this paper was done in part under a contract recommended by the Committee on Medical Research between the Office of Scientific Research and Development and Harvard University.

‡Instructor in medicine, Harvard Medical School; assistant physician, Thorndike Memorial Laboratory; assistant director, Second and Fourth Medical Services (Harvard) and junior visiting physician, Boston City Hospital.

§Research fellow, Harvard Medical School; research fellow, Thorndike Memorial Laboratory and assistant in medicine, Boston City Hospital.

¶Francis Weld Peabody Fellow and instructor in medicine, Harvard Medical School; research fellow, Thorndike Memorial Laboratory, and assistant in medicine, Boston City Hospital; tutor in biochemical sciences, Harvard University.

||Laboratory assistant, Thorndike Memorial Laboratory, Boston City Hospital.

||Associate in research medicine, Harvard Medical School; chemist, Thorndike Memorial Laboratory, Boston City Hospital.



vascular failure, the clinical criteria given in Table 1 were used without reference to the biochemical findings. The data chosen for the construction of the table were those obtained at a time when the peripheral vascular failure was present to the greatest extent. Variations in the blood chemical findings in certain typical patients are presented in the figures.

*The Relation of Biochemical Abnormalities to the Presence of Peripheral Vascular Failure*

**Abnormalities in carbohydrate metabolism.** Hyperglycemia was found in 9 of the 10 patients showing some degree of peripheral vascular failure. The tenth patient was poorly nourished. There was

Lactacidemia was found in all patients showing any degree of peripheral vascular failure, regardless of the clinical diagnosis. The correlation between the concentration of lactic acid in the circulating blood and the degree of peripheral vascular failure was striking. As might be predicted, in general the carbon dioxide content or the combining power varied inversely with the lactacidemia, although there was no evidence that the change in the alkaline reserve varied quantitatively with the amount of lactic acid. Other fixed organic acids were not determined. The lactic acid levels ranged from 4 to 20 milliequiv per liter of plasma or serum. In 2 cases (Cases 8 and 10) in which no peripheral

TABLE 1 Criteria Used in Estimating the Degree of Peripheral Vascular Failure \*

DEGREE OF PERIPHERAL VASCULAR FAILURE	RESPIRATION†	PULSE*	BLOOD PRESSURE	MENTAL STATE	CYANOSIS	EXTREMITIES	OLIGURIA
Minimal (+)	Normal	Thready and rapid	Slight fall	Restless and apprehensive	Lips or extremities or both	Pale and cool	None
Moderate (++)	Rapid and shallow	Thready and rapid	80/60 to 60/40	Apprehensive and confused	Lips or extremities or both	Cold and clammy	Questionable
Marked (+++)	Often Cheyne-Stokes or sighing	Thready and rapid	60/40 to 40/20	Confused to stuporous	Lips or extremities or both	Cold and clammy	Slight
Extremely marked (++++)	Often Cheyne-Stokes or sighing	Rapid, slow or unobtainable	40/0 to 20/0	Stuporous to comatose	Extremities mottled (extensive)	Cold and clammy	Moderate (often albumin, red cells and casts)

\*Temperature, nausea and vomiting were not used as general criteria because of the fluctuations due to causes other than peripheral vascular failure. The effect of the duration of the failure was taken into consideration in evaluating the biochemical findings (see Table 3).

†Unless modified by the clinical condition — for example, pneumonia.

minimal or no elevation of the blood glucose in the 2 patients in whom peripheral vascular failure was absent. One of these patients (Case 8) suffered from streptococcal pneumonia and recovered. The other (Case 10) was poisoned, presumably by barbiturates, and subsequently died.

There was no correlation between the height of the blood glucose and the degree of peripheral vascular failure. In 3 cases (Cases 3, 4 and 11) this type of comparison was impossible because of the necessity of administration of glucose for therapeutic reasons.

Glucose-tolerance determinations were made in 8 patients. In the patients who survived long enough, the blood-sugar levels had returned to normal prior to discharge. Glycosuria of slight degree was found in 2 patients. In none of the patients with abnormalities in the tolerance for glucose was the presence of diabetes mellitus discovered by the history, and in none of those who recovered was it shown by subsequent observations of the glucose level. In 3 patients, the ability to handle the added glucose was unimpaired, although the blood-sugar level was elevated. In the other 5 patients, the blood glucose was elevated at the end of two hours following a test dose of 25 gm intravenously.

vascular failure was present, the values were approximately normal, being 2 milliequiv per liter in each case.

**Abnormalities in the alpha amino nitrogen concentration of the plasma or serum.** The standard deviation from the mean of random determinations of the alpha amino nitrogen shown in the literature and in our own data is  $\pm 0.4$  mg. The mean for normal values is 4.1 mg per 100 cc of plasma.<sup>9,10</sup>

Although it is known that increases in alpha amino nitrogen occasionally occur in serum left in contact with cells,<sup>11</sup> determinations of this substance were made occasionally on serum as a matter of convenience. When this was done, the cells were removed as rapidly as possible and hemolysis was absent. For statistical purposes, no alpha amino nitrogen value was accepted as elevated that did not deviate from the mean by more than four times the standard deviation. In other words, it was accepted that the probability was only 1 in 1000 that an alpha amino nitrogen value above 6.0 mg per 100 cc of plasma or serum was due to chance alone. On this basis, 4 of the 10 patients with peripheral vascular failure had elevated alpha amino nitrogen values. These patients (Cases 3, 5, 7 and 12) had marked (++++) or extremely marked (++++) peripheral vascular failure.

At the same time it should be noted that the patients in Cases 3, 5 and 12 showed evidence of liver damage, as indicated by an increased prothrombin time and an elevated icterus index. Furthermore, the patient in Case 12 showed unmistakable evidence of cirrhosis of the liver at autopsy, and the patient in Cases 5 and 7 gave evidence of acute liver damage on histologic examination. The patient in Case 3 showed clinical evidence of previous liver damage. The great majority of patients with more than moderate (++) peripheral vascular failure, however, showed an increase in either the icterus index

Case 9, cyanosis and peripheral vascular failure were present but both the arterial and venous saturations were normal, which suggested that the circulating blood was a poor index of the anoxic state of the obviously cyanotic and probably anoxic tissue.

Studies of the Biochemical Abnormalities in Certain Cases

Typical cases from the group of patients with infection or various cardiovascular conditions and

TABLE 2 Clinical Data on Patients with Severe Medical Illnesses

CASE No	TYPE OF ILLNESS	AGE	SEX	DEGREE OF PERIPHERAL VASCULAR FAILURE	FINAL OUTCOME
Infection					
Pneumonia					
2	Pneumococcal (Type 7)	57	M	+	Recovered
9	Pneumococcal (Types 3 and 14)	62	F	+	Recovered
8	Streptococcal	19	M	0	Recovered
6	Undetermined	71	M	++	Died (not in peripheral vascular failure)
4	Meningitis (Type 14 pneumococcus)	60	F	++++	Died in peripheral vascular failure
5	Pericarditis (Type 1 pneumococcus)	68	M	++++	Died (not in peripheral vascular failure)
Cardiovascular disease					
1	Myocardial infarction with heart block	72	F	+	Recovered
7	Dissecting aneurysm	60	M	++++	Died in peripheral vascular failure
12	Mesenteric thrombosis	80	M	+++	Died in peripheral vascular failure
Poisoning					
10	Barbiturate (?)	32	M	0	Died (not in peripheral vascular failure)
11	Barbiturate (?)	30	F	++++	Died in peripheral vascular failure
3	Gastrointestinal hemorrhage	54	F	+++	Died in peripheral vascular failure

or the prothrombin time, or both, without any significant increase in the plasma alpha amino nitrogen.

**Blood oxygen and arteriovenous oxygen differences (femoral).** There is no evidence from the data in Table 3 that there is any degree of correlation between the oxygen content or saturation of the arterial or venous blood and the degree of peripheral vascular failure. Five patients with marked (++) or extremely marked (++++) peripheral vascular failure, however, showed an arterial oxygen saturation of 85 per cent or less, 100 per cent hemoglobin being considered equivalent to 20.9 vol of oxygen per 100 cc of blood. The patient in Case 3 had a marked anemia from blood loss, as well as a marked unsaturation of the remaining hemoglobin. In all other cases, the patients had either a normal or a somewhat elevated hemoglobin concentration. The elevation of the hemoglobin did not show a great deal of hemoconcentration in relation to the severity of the peripheral vascular failure. Indeed, the patient in Case 10, who had no peripheral vascular failure, had the highest hemoglobin concentration — 117 per cent. The patients in Cases 9 and 10 had low arteriovenous oxygen differences. In

a case of probable barbiturate poisoning will be presented. Each of these patients had at least marked (++) peripheral vascular failure in association with the severe illness.

CASE 5 A 68-year-old man with pericarditis (pneumococcus, Type 1), peripheral vascular failure estimated at ++++

This patient had been suffering from a vague illness associated with epigastric pain and constipation of 10 days' duration. He was seen by his physician on the day previous to admission, at which time the pulse, temperature, heart and lungs were reported to be normal. Shortly before admission he became extremely dyspneic and mentally confused. Examination on admission revealed a well developed and well nourished elderly man suffering from marked respiratory distress. The blood pressure was unobtainable. The femoral pulse was 180, the respirations 40, and the rectal temperature 97°F. The patient was mentally confused, irrational and apprehensive. The skin was cold and dry, with mottled cyanosis of the extremities as well as of the lips and nail beds. Examination of the lungs revealed medium moist rales throughout both lung fields. On percussion the heart was 13 cm to the left and 4 cm to the right of the midsternal line. The sounds were distant and muffled, without murmurs or friction rubs. The radial pulse was not palpable, but the femoral pulse was obtainable and was markedly paradoxical. A clinical diagnosis of pericardial effusion was made, which was consistent with the electrocardiographic tracings. The patient was accepted for biochemical study and was classified as having ++++ peripheral vascular failure. During the period of unobtainable blood pressure, marked

biochemical abnormalities were observed (Figs 1 and 2). The blood glucose was markedly elevated (143 mg per 100 cc). The serum lactic acid was 14.6 milliequiv per liter, and the carbon dioxide content of the serum was reduced to 8 millimols per liter. The serum nonprotein nitrogen was elevated to 276 mg per 100 cc, and the alpha amino nitrogen was at the extremely high level of 20.0 mg. The arterial

of purulent fluid was removed from the pericardium. A catheter was inserted into the pericardium and used for irrigation with penicillin.

Immediately after the first pericardial tap, the blood pressure rose to 70/50 and there was marked relief of respiratory distress. The second blood sample was obtained 7 hours after the first and 5 hours after the pericardial tap. At that

TABLE 3 Biochemical Data at Time of Greatest Peripheral Vascular Failure

CASE No	PERIPHERAL DEGREE	VASCULAR FAILURE ONSET	DURATION	GLUCOSE	LACTIC ACID	HEMOGLOBIN	CO <sub>2</sub> CONTENT	CO <sub>2</sub> COMBINING POWER
			hr	mg/100 cc	mE/l	%	mM/l	mM/l
4	++++	Slow	12	234*	20	93	12	—
7	++++	Acute	2	332	16	83	—	17
5	++++	Slow	?	143	15	84	8	—
3	++++	Acute	12	552*	14	36	15	—
11	++++	Slow	36	370*	12	101	11	—
12	+++	Slow	?	122	8	101	36	—
6	+++	Slow	?	79	6	102	—	24
1	++	Acute	16	178	6	88	—	21
2	+	Slow	54	122	5	81	—	26
9	+	Slow	?	146	4	105	25	—
10	0	—	—	97	2	117	24	—
8	0	—	—	86	2	84	—	19

\*Glucose administered parenterally.

oxygen content was 14.0 vol per cent, which in the presence of a hemoglobin concentration of 84 per cent indicated a saturation of 79 per cent. The Quick prothrombin time of the initial blood was prolonged to 35 seconds (normal, 21 seconds). The icterus index was 12.5.

Shortly after the initial blood was taken, a pericardial tap was performed and 150 cc of yellowish-green purulent

time there was no evidence of peripheral vascular failure, nor did it later recur. The blood glucose on this sample had risen to 172 mg per 100 cc. In subsequent samples it fluctuated between 155 and 225 mg until the 3rd hospital day.

A glucose-tolerance test was made from the 4th to the 6th hour after the initial blood was taken. It was grossly abnormal. Unfortunately, the blood glucose was at a high

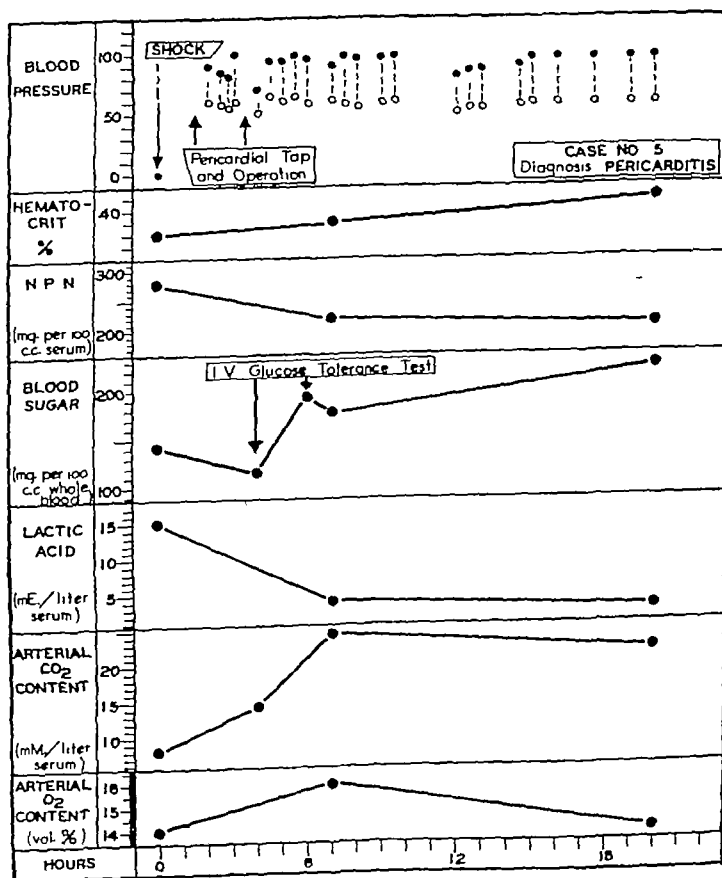


FIGURE 1

fluid was removed. This fluid and a simultaneous blood culture showed the presence of Type 1 pneumococcus. Twenty-five thousand units of penicillin in 25 cc of saline solution was instilled in the pericardium by a second tap. A pericardial exploration was made, at which time a further 200 cc

level at that time and continued to rise during the subsequent 5 hours. The interpretation of the finding is therefore extremely difficult.

A sample of heart blood taken just prior to death on the 4th day gave a low level of glucose (39 mg per 100 cc). The

serum lactic acid level fell promptly after return of the blood pressure to relatively normal levels, falling from the initial level of 14.6 to 4.0 milliquiv per liter. Subsequent levels taken at varying intervals of time until death gave values of 3.2 and 3.6 milliequiv.

The carbon dioxide content rose rapidly from the initial level of 8 millimols per liter to 24.5 millimols as peripheral

the patient remained mentally confused, with a uremic odor on the breath and a uremic frost on the face, until death.

*Autopsy.* The kidneys were grossly normal. They stripped easily and were of average size and weight. Histologically there were no essential abnormalities except acute edema and congestion. The liver microscopically revealed marked central necrosis, but it was thought that the morphologic

TABLE 3 (Concluded)

CASE No	OXYGEN SATURATION		ARTERIOVENOUS OXYGEN DIFFERENCE	ICTERUS INDEX	ALPHA AMINO NITROGEN	QUICK PROTHROMBIN TIME†	OUTCOME	LIVER DISEASE AT AUTOPSY
	ARTERIAL	VENOUS						
	%	%	vol %		mg/100 cc	sec		
4	80	11	14	10	4.7 (plasma)	38	Died	No autopsy
7	—	—	—	6	6.5 (plasma)	—	Died	+ (acute)
5	70	—	—	13	20.0 (serum)	35	Died	+ (acute)
3	65	—	—	75	7.3 (serum)	53	Died	No autopsy
11	81	—	—	9	5.2 (serum)	46	Died	+ (acute)
12	50	32	6	11	6.1 (serum)	30	Died	+ (chronic)
6	—	—	—	6	4.1 (plasma)	31	Died	+ (acute)
1	—	—	—	4	3.9 (plasma)	19	Living	
2	—	—	—	13	2.9 (plasma)	25	Living	
9	91	79	4	4	4.0 (serum)	23	Living	
10	74	71	1	4	—	—	Died	+
8	—	—	—	6	4.1 (plasma)	26	Living	

†Normal 21 to 26 seconds

vascular failure subsided, and remained at these normal levels for the 24 hours over which observations were made. There was no important statistical change in the oxygen content, although the oxygen saturation rose to 91 per cent after the operation but in 24 hours had fallen to 75 per cent of saturation.

The nonprotein nitrogen remained above 200 mg per 100 cc. until death, but the serum alpha amino nitrogen fell

findings were consistent with an acute rather than a chronic change.

*CASE 7.* A 60-year-old man with dissecting aneurysm of the aorta, peripheral vascular failure estimated at ++++

Three hours before admission the patient developed a dull, aching pain at the anterior base of the neck, without radiation. Shortly afterward he experienced a dull, aching, "smother-

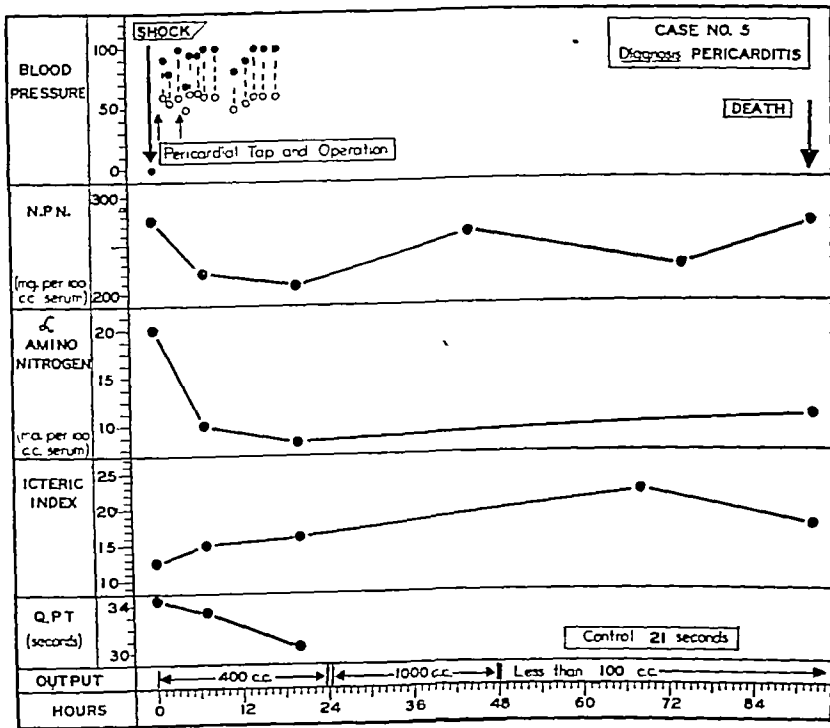


FIGURE 2

promptly after operation from 20 to 10 mg, at which high level it continued until the patient's demise. The icterus index and the prothrombin time both remained elevated until death. Oliguria was present from admission and gradually became progressive. The clinical picture of uremia was present and was progressive. In spite of the improvement in the respiratory distress and peripheral failure,

ing" pain over the precordium. This was followed by collapse and loss of memory until after arrival at the hospital. On recovery of consciousness, the patient complained of abdominal cramps and a desire for defecation. At no time was there radiation of pain. The past history revealed excellent health, without evidence of diabetes or kidney, liver or heart disease and was irrelevant, with the exception of a

biochemical abnormalities were observed (Figs 1 and 2) The blood glucose was markedly elevated (143 mg per 100 cc) The serum lactic acid was 14.6 milliequiv per liter, and the carbon dioxide content of the serum was reduced to 8 millimols per liter The serum nonprotein nitrogen was elevated to 276 mg per 100 cc, and the alpha amino nitrogen was at the extremely high level of 20.0 mg The arterial

of purulent fluid was removed from the pericardium A catheter was inserted into the pericardium and used for irrigation with penicillin Immediately after the first pericardial tap, the blood pressure rose to 70/50 and there was marked relief of respiratory distress The second blood sample was obtained 7 hours after the first and 5 hours after the pericardial tap At that

TABLE 3 Biochemical Data at Time of Greatest Peripheral Vascular Failure

CASE No	PERIPHERAL DEGREE	VASCULAR FAILURE ONSET	DURATION hr	GLUCOSE	LACTIC ACID	HEMOGLOBIN	CO <sub>2</sub> CONTENT	CO <sub>2</sub> COMBINING POWER
				mg / 100 cc	mE / l	%	mM / l	mM / l
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time there was no evidence of peripheral vascular failure, nor did it later recur The blood glucose on this sample had risen to 172 mg per 100 cc In subsequent samples it fluctuated between 155 and 225 mg until the 3rd hospital day A glucose-tolerance test was made from the 4th to the 6th hour after the initial blood was taken It was grossly abnormal Unfortunately, the blood glucose was at a high

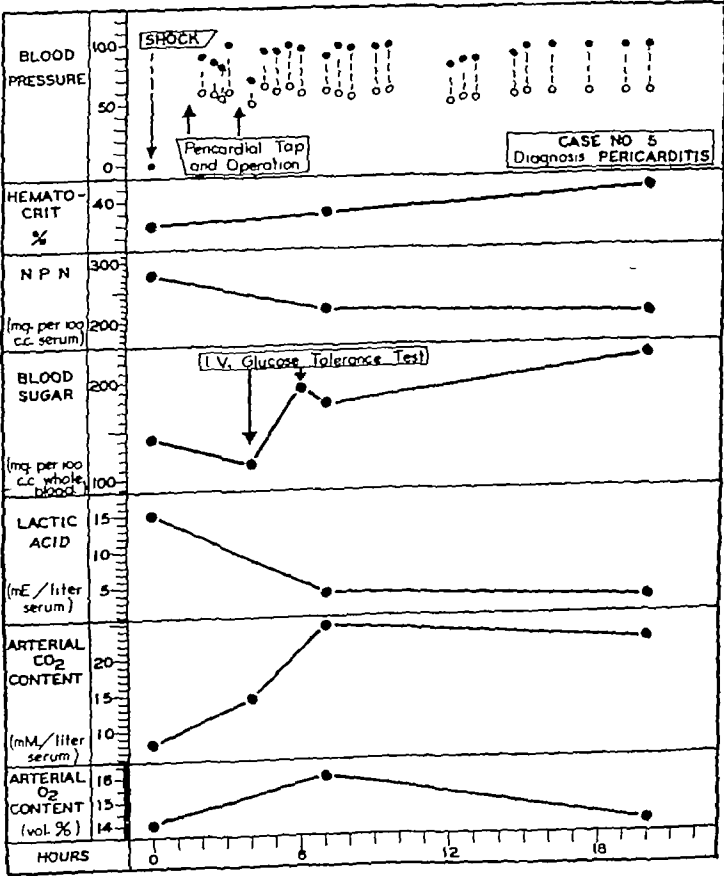


FIGURE 1

fluid was removed This fluid and a simultaneous blood culture showed the presence of Type 1 pneumococcus Twenty-five thousand units of penicillin in 25 cc of saline solution was instilled in the pericardium by a second tap A pericardial exploration was made, at which time a further 200 cc

level at that time and continued to rise during the subsequent 5 hours The interpretation of the finding is therefore extremely difficult A sample of heart blood taken just prior to death on the 4th day gave a low level of glucose (39 mg per 100 cc) The

were suggestive of anterior infarction, with probable septal involvement. Signs of peripheral vascular failure became evident, and the patient was transferred for study. The blood pressure had fallen from 138/98 to 80/50. The extremities were cold, and there was marked peripheral vasoconstriction. One hour later, the first biochemical studies were made, the blood pressure at that time being 90/70 and varying between this level and 80/50 for the next 6 hours, at which time the second blood samples were collected.

Twenty-four hours after the initial blood was taken, the signs of complete heart block cleared and the blood pressure rose to 100/60. Signs of peripheral vascular failure disappeared. The patient gradually improved and was discharged 9 weeks after entry.

The blood sugar on the initial blood was elevated to 195 mg per 100 cc. and remained above 150 mg for the first 6 days (Fig. 3). Following this, the blood-glucose level gradually declined, and on the 24th hospital day it was normal.

The prothrombin time and the icterus index remained normal throughout the hospital stay. With the exception of the blood-glucose level, the biochemical abnormalities referable to carbohydrate metabolism were minimal.

Two of the 12 patients studied (Cases 8 and 10) showed no evidence of peripheral vascular failure. Case 10 was one of probable barbiturate poisoning, and the patient died 12 hours after admission. A complete blood study was made seven and a half hours prior to death. A glucose-tolerance test showed an abnormal tolerance. This was the only biochemical abnormality observed. An interesting phenomenon was the presence of marked fibrinolysis in the blood five and a half hours prior to death.

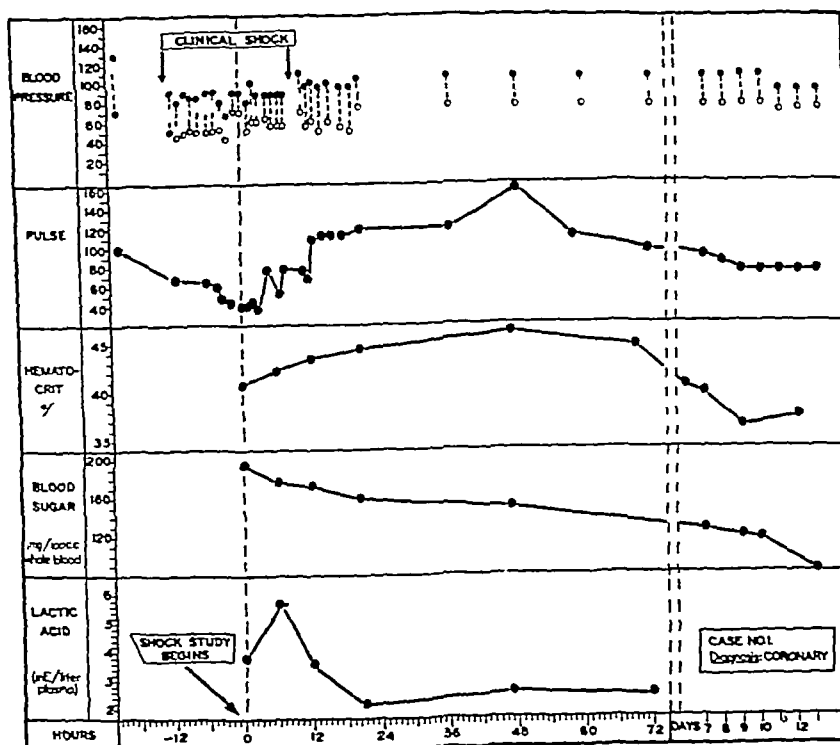


FIGURE 3

Glucose-tolerance tests were slightly abnormal during the period when hyperglycemia was present. A glucose-tolerance test after discharge was normal, and the fasting blood sugar had been within normal range from the 19th day. Studies of this patient were discontinued on the 24th day.

The plasma lactic acid was 4 milliequiv per liter on the initial sample, rising to 6 milliequiv in 6 hours. Thereafter it declined, and at the time of the last sample, 70 hours after the study had commenced, it had reached a level of 2.5 milliequiv. The carbon dioxide combining power remained within normal limits throughout the study.

The nonprotein nitrogen was elevated to 80 mg per 100 cc on the initial blood plasma sample and rose to 135 mg 47 hours later. Seven days later, it had reached a level of 173 mg, and thereafter it slowly declined, reaching 58 mg on the 24th day after admission. The alpha amino nitrogen showed no statistically significant increase. The urine output during the first 2 days was small but not measured. It was 650 cc on the 3rd day and gradually increased to normal volume by the 5th day. Single urine specimens had specific gravities ranging from 1.002 to 1.012 during the first 8 days following admission. The sediment showed many white cells and occasional red cells and epithelial cells but no casts.

This blood sample was collected during a period of apnea, which terminated following the administration of oxygen and picrotoxin. The icterus indices of the patients in Cases 8 and 10 were normal, and the prothrombin time in Case 8 was normal.

The patients not described in detail follow similar patterns of response to those outlined above. The clinical manifestations in each case varied considerably, but the biochemical findings differed only in degree.

### DISCUSSION

At the outset of this discussion, it must be emphasized that the clinical evaluations were arrived at without reference to the biochemical findings. In the final analysis, the data were arranged according to biochemical findings and the clinical interpreta-

single attack of "angina" 15 years previously. A brother was known to have died of a "ruptured aorta."

Physical examination revealed a well developed, well-nourished man complaining of moderate precordial and abdominal pain. The pulse was 110, the rectal temperature 97°F, the respirations 25, and the blood pressure 40/20. The extremities were cold, clammy and cyanotic, and a mottled blue discoloration was observed over the flanks. The lungs were clear, but breathing was slightly labored. There was slight venous distention in the neck. The heart was not enlarged, but the sounds were distant and indistinct. The radial pulse was not palpable. The abdomen was soft, but some periumbilical tenderness could be elicited on deep palpation. The electrocardiographic record showed sinoauricular tachycardia and a slightly abnormal ST segment, which was interpreted either as being due to the heart rate or as being consistent with the presence of myocardial disease. A diagnosis of dissecting aneurysm of the aorta was made.

Although the patient received 1500 cc of saline solution, 500 cc of plasma and coramine, caffeine, morphine and oxygen, he remained cyanotic, with no obtainable blood pressure after the 1st hour. Seven and a half hours after admission he became irrational, and 2 hours later he died.

Only one set of blood samples was obtained for analysis. These were collected immediately after admission, when the blood pressure was 40/20. Blood was obtained for glucose determinations alone on two occasions when the blood pressure was unobtainable. The blood sugar on the initial sample was 332 mg per 100 cc and increased during the next 3 hours to 446 mg. The blood lactic acid was at the high level of 15.7 milliequiv per liter of plasma. The carbon dioxide combining power was 17 millimols per liter. A glucose-tolerance test showed the initial blood glucose to be 446 mg, 2 hours after the injection of 25 gm of glucose it was 351 mg. During this period the patient also received 500 cc of therapeutic plasma containing not less than 20 gm of glucose. The nonprotein nitrogen was normal, but the plasma alpha amino nitrogen on the initial sample was elevated to 6.5 mg per 100 cc.

Prothrombin times were not obtained, and the icterus index was normal.

**Autopsy.** The liver showed acute focal necrosis, and a dissecting aneurysm of the aorta was found.

**CASE 11.** A 30-year-old, unmarried woman with presumptive evidence of poisoning by a barbiturate, peripheral vascular failure estimated at ++++

The patient had been treated for 2 months prior to entry for a "nervous breakdown," but was in apparent good health the day before admission. During that night the patient was noticed to be breathing heavily. In the morning she was comatose and was brought to the hospital in this condition. The only sedative known to be in her possession was Nembutal.

The past history showed no evidence of diabetes, hypertension or kidney or liver disease. There was no history of trauma, habitual taking of drugs or organic disorder of the central nervous system.

On admission, the temperature was 100°F, the pulse 120, the respirations 26, and the blood pressure 80/60. The patient was comatose and could not be aroused. The breathing was labored, and the skin was cyanotic and cold. The patient's general appearance was described as moribund. Over the back and lower extremities there were numerous first-degree and second-degree burns covering less than 3 per cent of the total body surface, apparently due to the application of hot-water bottles while the patient was in a comatose state. She was treated with oxygen, coramine, caffeine and unknown amounts of picrotoxin. Intravenous fluids were given, together with therapeutic amounts of sulfadiazine. A lumbar puncture was performed. The spinal-fluid pressure was equivalent to 490 mm of water, the total protein was 30 mg per 100 cc., and there were 1 white cell and 30 red cells per cubic millimeter.

Thirty-three hours after admission, when the patient was still comatose, additional clinical findings were obtained. The blood pressure was unobtainable. The extremities were cold and cyanotic, although the patient had been receiving oxygen since admission. There were medium and coarse moist rales throughout the lung fields. Examination of the abdomen revealed moderate muscle spasticity and flexion of the legs on deep abdominal pressure. Neurologic examination revealed dilated pupils that reacted slowly to light.

Reflexes were absent with the exception of a gag response, which was inconsistently observed.

Lumbar puncture was repeated and showed a normal pressure. The fluid contained only a few red cells. The patient was catheterized, and 80 cc of urine was obtained during the next 8 hours. The patient died 41 hours after admission. A medicolegal post-mortem examination was performed.

The first blood sample was taken 33 hours after admission, when the blood pressure was unobtainable. The blood glucose was 369 mg per 100 cc and in 2½ hours rose to 586 mg. So far as the records show, no glucose was administered after the study was started. Just before death, 8 hours after the initial blood was taken, a sample of heart blood showed a glucose level of 293 mg per 100 cc.

The serum lactic acid on the initial sample of blood was markedly elevated (11.8 milliequiv per liter), and the carbon dioxide content of the serum was reduced (15 millimols). The lactic acid level fell slowly, being 8.4 milliequiv 3 hours later and 7.2 milliequiv shortly before death. A further observation of the carbon dioxide content showed a slight fall (13 millimols per liter) 2 hours after the initial sample.

The nonprotein nitrogen was 66 mg per 100 cc on the initial sample and rose to 91 mg at the time of death. The alpha amino nitrogen remained within normal limits throughout the period of study. The total urine output during the 41 hours following admission was approximately 290 cc, and the specific gravity was 1.030.

The arterial oxygen saturation was 81 per cent on the initial sample of blood and had risen to 87 per cent 3 hours later. The icterus index was normal throughout the course. The prothrombin time was distinctly prolonged, being 46 and 54 seconds (normal 24 seconds).

**Autopsy.** The post-mortem findings were superficial burns of the skin, submucosal hemorrhages of stomach and small intestine, bronchopneumonia (right) and acute central necrosis of the liver.

The foregoing cases represent severely ill patients in whom the component of peripheral vascular failure was extreme. The following case represents a severely ill patient in whom peripheral vascular failure was minimal (+).

**CASE 1.** A 72-year-old woman with myocardial infarction and complete heart block, peripheral vascular failure estimated at +.

This patient was admitted 1 year previous to the present entry with a possible acute diverticulitis. At that time there was no evidence from either a clinical or a biochemical viewpoint of any abnormality in the carbohydrate metabolism. Two years before the present admission, there was a gradual onset of dyspnea, palpitation and ankle edema, which never reached severe proportions. Two months before admission, the patient had a 3-hour attack of substernal pain and a choking sensation, which did not recur until 3 days before admission. This attack followed exertion and disappeared at rest. On the evening of admission, a severe substernal pain which was described as crushing, occurred. It radiated to the right shoulder and down the right arm. The patient vomited twice and had chilly sensations, with perspiration. Her physician gave her an injection of an unknown therapeutic agent, and she was admitted to the hospital 4 hours later.

Physical examination revealed a moderately obese woman in obvious substernal distress. The pulse was 96, and the blood pressure 130/98. The patient was mentally clear but slightly drowsy. The skin was warm and dry. There was no evidence of increased venous pressure in the neck. The lungs were clear to percussion, with some dry inspiratory rales posteriorly at both bases. The apex impulse of the heart was heard at the midclavicular line, and there were no murmurs. The sounds were distant. There was some tenderness in the right upper quadrant of the abdomen. Minimal ankle edema was present. Electrocardiographic records showed changes suggestive of an active process involving the anterior heart surface.

On the following day, the patient developed a complete heart block. The electrocardiographic findings at that time were as follows: auricular rate, 103, ventricular rate, 32-36, with evidence of right bundle-branch block. These findings

changes of the liver at autopsy. At the present time the possibility of hepatic function conditioned by decreased hepatic blood flow due to peripheral vascular failure as a cause of the increased alpha amino nitrogen observed in this series cannot be ruled out. The extremely high plasma alpha amino nitrogen in Case 7 (20 mg per 100 cc) requires some comment. This patient during the hospital stay had a plasma nonprotein nitrogen greater than 200 mg per 100 cc. The alpha amino nitrogen of blood plasma is usually 5 per cent of the total nonprotein nitrogen. One might therefore expect in this case that with a normal distribution of the nonprotein constituents of the plasma there would be an increase in the alpha amino nitrogen. It should be noted, however, that following the disappearance of peripheral vascular failure the alpha amino nitrogen fell abruptly from 20 to 10 mg per 100 cc, at which level it remained until death, although there was no parallel fall in the nonprotein nitrogen.

Azotemia has been found in several of the patients studied. In 1 case it was a serious complication. We<sup>6</sup> have commented previously and elsewhere<sup>17</sup> on the fact that the azotemia found in certain traumatic conditions was due to two components — an increased production of nitrogen and an impaired kidney function. Otherwise we<sup>5</sup> have found a temporary azotemia associated with an oliguria that disappears when the normal urine output is restored. In most cases the azotemia found in the present series was of the latter character. In Case 5, in which the nonprotein nitrogen was over 200 mg throughout the patient's hospital stay and the signs of uremia were severe and progressive, only a minimal kidney lesion was found macroscopically or microscopically at post-mortem examination. Minor kidney impairment was indicated by urinalysis. In this patient also there is therefore a possibility that the azotemia was in part extrarenal.

The findings in this small series of cases indicate that the biochemical abnormalities accompanying peripheral vascular failure in patients suffering from severe medical illnesses are similar to those found in various traumatic conditions, hemorrhage and anoxia. Although the primordial cause is not known, it is not improbable that when peripheral vascular failure occurs it does so in association with tissue anoxia. Under these circumstances, it is suggested that there is a marked increase in glycolysis and possibly gluconeogenesis resulting in hyperglycemia. The production of lactic acid in amounts greater than the liver can transform or greater than can be excreted results in a marked lactacidemia. If there is a concomitant disturbance in hepatic function, as the present data indicate, the lactacidemia may be still further enhanced. Usually, although alpha amino nitrogen is an intermediate in gluconeogenesis, the amount of alpha amino nitrogen formed is easily handled by the

normal liver. Alpha amino nitrogen levels in the blood do not ordinarily increase with increases in nitrogen turnover. If, however, as a result of the presence of peripheral vascular failure there is a marked increased protein catabolism, with a failure of deamination due to an impaired liver function, an increase in alpha amino nitrogen is not improbable.

It has been reported that patients with severe medical illnesses may suddenly develop "diabetes" or if previously diabetic may have an exacerbation of their disease.<sup>17</sup> It is not improbable that if the component of peripheral vascular failure is present such observations may represent additional cases of the type of biochemical lesion reported here.

Cardiac infarction has been reported to be accompanied by abnormalities in carbohydrate metabolism of a transitory nature in nondiabetic individuals.<sup>18-20</sup> Eckerström<sup>18</sup> definitely relates the occurrence of such abnormalities to the presence of shock.

#### SUMMARY

The biochemical changes associated with peripheral vascular failure accompanying severe, acute medical illnesses are described.

They consist of hyperglycemia, lactacidemia and a fall in the bicarbonate reserve. The oxygen saturation of the peripheral blood is reduced. The alpha amino nitrogen of the blood plasma is often elevated. There is usually a lengthening of the prothrombin time, and an elevation of the icterus index.

There is a marked correlation between the degree of the peripheral vascular failure and the profoundness of the biochemical abnormality.

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tions were added. Had the reverse procedure been carried out, — namely, an arrangement of the cases on the basis of the degree of involvement with peripheral vascular failure, — the biochemical data would have presented the same pattern as is set forth in this report. The choice of lactic acid levels as the basis for the biochemical arrangement of the data on abnormal carbohydrate metabolism was made because it was the only carbohydrate component that was in no wise directly altered by the necessary therapeutic procedures.

The method of grading the degree of peripheral vascular collapse is quite arbitrary. It is not offered as representing a desirable method, but simply indicates a justification for the classification of peripheral vascular failure used in this presentation. A much larger series of cases would be required to give it greater value. By its use, however, two clinicians were able independently to agree on the status of the clinical material. With the use of these criteria, the data show clearly that there is a high degree of correlation between the existence of peripheral vascular failure and the presence of marked abnormalities in the carbohydrate metabolism of human subjects. This is true regardless of the type of medical illness studied, of which the peripheral vascular failure is a component. Furthermore, on the basis of lactic acid determinations this small series of patients indicates a close parallel between the degree of peripheral vascular failure and the profoundness of abnormality.

In two cases in which peripheral vascular failure was absent, the disturbance of carbohydrate metabolism was minimal or absent. It is true that consideration must be given to other factors, such as the patient's age and the severity of the illness. The latter is difficult to evaluate, since no patient was studied who was not considered severely ill at the outset. The question of age is more pertinent, since it is known that abnormalities in carbohydrate metabolism occur oftener in the older age groups than in the younger ones. This is notably true in the case of diabetes mellitus.<sup>12</sup> The findings in the 2 cases of presumptive barbituric poisoning (Cases 10 and 11), however, offer some support to the belief that age is not the only determinant. These patients were both in the early thirties, and both had so severe an illness that they died. On the initial blood samples alone, however, the patient in Case 11 had marked disturbance in carbohydrate metabolism, as indicated by hyperglycemia, lactic acidemia and acidosis, whereas the patient in Case 10 showed no observable changes in these biochemical findings. The only significant difference between the two patients was that in Case 10 peripheral vascular failure was entirely absent, whereas in Case 11 it was severe and had been present for some length of time. The patient in Case 8, who was nineteen years old, also showed no peripheral vascular

failure and only minimal abnormalities in carbohydrate metabolism.

Although such abnormalities in the glucose-tolerance curves showed in the main an intolerance for glucose, many of the curves were not subject to interpretation owing to the rapid and spontaneous fluctuations in glucose at the time of observation. In any event, although abnormalities in glucose tolerance were of the diabetic type, there was no evidence of clinical diabetes in any patient. Furthermore, in the patients who recovered from their illnesses there was evidence of a return of the carbohydrate metabolism to normal. Further follow-up studies will be made and reported later.

Concerning the cause of the abnormality in carbohydrate metabolism, there is no evidence to be drawn from this report. In a previous report some of the most widely accepted theories were reviewed.<sup>6</sup> One may speculate on one contributing factor in these patients. Hematocrit and protein data show that diminution of blood volume although sometimes present was never great and probably could not account for the degree of peripheral vascular failure found. Anoxia is known to produce such biochemical changes as are given here.<sup>13,14</sup> In the production of such an anoxia a reduction in cardiac output may play an important role. On the basis of laboratory and clinical findings, at least three types of anoxia were obviously present in these patients — anoxic anoxia (Case 12), anemic anoxia (Case 3) and presumably stagnant anoxia in the cases with marked cyanosis.

It is of considerable practical importance that femoral venous oxygen determinations give no clue to the state of oxygenation in the tissues in the latter cases. This may well be due to the presence of arteriovenous shunts in the periphery, as first proposed by Cannon<sup>15</sup> and recently postulated by Glenn and his associates.<sup>16</sup> It is significant that oxygen content, saturation and femoral arteriovenous oxygen differences in the few patients studied failed to show a high degree of correlation with the degree of peripheral vascular failure.

That functional disturbances of the liver exist in patients with a marked degree of peripheral vascular failure is inescapable. High icterus indices or prolonged prothrombin times, or both, were present in all patients showing more than the mildest form of peripheral vascular failure, regardless of the disease from which the patient suffered. In some cases the existence of early central necrosis was found in the liver at autopsy.

The alpha amino nitrogen was raised to levels of statistical significance in Cases 3, 5, 7 and 12. In each case there was profound peripheral vascular failure, but in Cases 3, 5, and 12 there was also a strong indication of derangement of liver function. In Case 7, in which there was normal icterus index and no determination of prothrombin time was made, there was evidence of acute degenerative

been passed. Certain minimum standards of early diagnosis must be provided.

In the modern enthusiasm for radiologic diagnosis, the venogram has received ardent support from many students of venous diseases, among them Fine and Sears,<sup>16</sup> Starr, Frank, and Fine,<sup>17</sup> dos Santos,<sup>18</sup> Bauer,<sup>19</sup> Welch, Faxon, and McGahey,<sup>20</sup> DeBakey, Schroeder and Ochsner<sup>21</sup> and Dougherty and Homans.<sup>22</sup> On the other hand, there are many investigators who question the value of venography, these include Bancroft,<sup>10</sup> deTakats,<sup>1, 23</sup> and Allen, Linton and Donaldson.<sup>7</sup> It is perhaps significant that some of the advocates of this type of examination in the past have become increasingly more critical in more recent years. Thus, Fine<sup>24</sup> in a recent article shows a considerable decrease of enthusiasm for the procedure. Homans<sup>25</sup> recently called venograms disappointing. Welch and Faxon<sup>12</sup> admit that cases occur in which clinical signs of venous occlusion precede the positive findings of the venogram.

The objections to venography offered by the workers opposed to its use are as follows. There is a definite risk of either initiating or increasing the venous thrombosis. The examination is usually moderately expensive and requires material and apparatus that are not always available. False-negative reports occur in as many as 33 per cent of cases and are especially frequent in the early stages of the disease, when phlebothrombosis is actually most dangerous. There is a large group of venograms in which the interpretation of findings is extremely difficult, especially those of the legs, in which physical signs are minimal — the very cases in which venograms would be most desirable if they were reliable. Lastly, venospasm is frequently impossible to differentiate from organic occlusion. It is probable that a paravertebral sympathetic novocain block preceding the venogram would remove this limitation.

In addition to these objections, there are normally present at least six deep veins of the lower extremity — the paired anterior tibials, the posterior tibials and the peroneal veins. Although venography has been a frequent procedure at this hospital, I have never seen a venogram, either pathologic or normal, in which it was possible to outline these six trunks. If the experience of other observers has been similar, this indicates the extremely limited value of venography in the diagnosis of early phlebothrombosis of the calf veins.

The almost universal acceptance of the sign described by Homans<sup>22</sup> as one of value in diagnosing venous occlusion is subject to some question. Reasoning that this maneuver stimulates too many things at one time, I have had an interesting experience in the last year or so. I have tried this maneuver in 88 patients who had other pathologic conditions not related to phlebitis and in whom phlebothrombosis was not suspected, either at the

time of examination or later. This series included 4 patients with contusions of the calf, 6 with fractures of the tibia or fibula, 1 with osteogenic sarcoma of the tibia, 3 with osteomyelitis of the tibia, 2 with septic arthritis of the knee, 2 with septic arthritis of the ankle, 3 with myofasciitis of the calf muscles, 15 with recent ankle sprains, 2 with lacerations of the calf muscles, 1 with a recent penetrating wound of the calf, 4 with recent poliomyelitis, 6 with cellulitis of the subcutaneous tissue of the calf, 5 with various types of acute meningitis, 2 with ruptured intervertebral disks, 4 with "sciatica" of undetermined cause, 7 with peripheral neuritis, 6 with occlusion of the popliteal artery, 1 with scleroderma, 12 adolescents and young adults with ankle fractures whose casts had just been removed, 1 with hysteria and 1 with heat cramps. All these patients demonstrated both limitation of passive dorsiflexion of the ankle and pain in some portion of the calf on performance of this test. Furthermore, none of them subsequently developed emboli or any further local signs compatible with venous occlusion.

Evidence that the incidence of false-negative reactions is high is afforded by Allen's<sup>14</sup> experience, in which only 59 of 202 patients showed Homans's sign in the early phases, although he considers the test as absolutely diagnostic when present — an opinion in which I cannot concur.

In view of the severe limitations of the venogram and the Homans test in the early phase of phlebothrombosis, and the further fact that the classic picture of this malady is actually the late one and is thus valueless in the incipient stage, the question of how one is to make the early diagnosis arises.

It has been noted at this hospital that tenderness of the posterior calf, either localized or extensive and following the course of the deep veins, is almost always the first local sign of venous thrombosis, as has been reported by Veal and Hussey.<sup>15</sup> With the exception of the infrequent cases in which pulmonary embolus precedes local signs of any kind, the stage in which tenderness is the only sign is the ideal time to make the diagnosis and of course to perform a proximal ligation. We see great numbers of such patients owing to the daily examination of the calves of patients whose age, general condition and confinement to bed for long periods make them peculiarly liable to this complication.

Obviously, however, not every patient developing tenderness along the posterior calf has venous disease as the cause. If there were a method of knowing that the tenderness elicited was venous, the diagnosis at this stage would be greatly simplified. In actual practice, pressure along the posterior calf causing pain permits the same diagnostic fallacies as those encountered in the Homans test, because, again, many structures are being simultaneously compressed. The skin, subcutaneous tissue, fascia and large calf muscles are, however, capable of being tested as a group aside from the

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## THE EARLY DIAGNOSIS OF PHLEBOTHROMBOSIS\*

WILLIAM R. MOSES, M D †

WASHINGTON, D C

NOTHING so captivates the medical mind as the prevention of catastrophe by a simple method. Thus may be explained the rapidly increasing popularity of proximal ligation of thrombosed veins for the prevention of pulmonary embolism. Indeed, there must be few surgeons who have not witnessed the shockingly sudden transition of a happy convalescent into a patient rapidly dying from this totally unexpected disaster. Nor is the picture of so-called "thromboembolism" infrequent. Neumann<sup>2</sup> in a study of 165 random cadavers, found that 65 per cent of them demonstrated ante-mortem venous thromboses of the lower leg, 52 per cent of which were bilateral. He also stated that 12 per cent of all these thromboses were associated with massive pulmonary embolism and that an additional 34 per cent were associated with multiple nonfatal emboli. Rössle<sup>3</sup> reports that 11 per cent of routine autopsies of patients over twenty years of age showed thromboses of the femoral vein and that 30 per cent of these had developed massive pulmonary embolism. Hosor<sup>4</sup> attributes 1 death per 1000 hospital population to pulmonary embolus.

Pilcher<sup>5</sup> assigns to embolus 1 death following every 1000 surgical operations. Henderson<sup>6</sup> states that it is the cause of 6 per cent of all postoperative deaths. Allen,<sup>7</sup> quoting Davis of the Massachusetts General Hospital, claims that 3 deaths from embolus followed every 1000 operations. Hunter and his associates<sup>8</sup> attribute 3 per cent of all hospital deaths to pulmonary emboli, and find that 53 per cent of bedridden patients develop deep-vein thrombosis of the legs. McCartney,<sup>9</sup> reviewing over 25,000 autopsies, found 2.7 per cent of the deaths to have been due to emboli in the lungs and estimated that 5.3 per cent of postoperative deaths resulted from this complication. Bancroft<sup>10</sup> expects pulmonary embolism in 10 per cent of victims of phlebothrombosis. Miller and Rogers<sup>11</sup> encountered 7 deaths in 206 patients with clinically recognizable thrombophlebitis.

There thus remains little doubt of both the ubiquity and the seriousness of this condition. At the present time, although there are notable cham-

pions of the medical management of these non-inflammatory venous thrombi, the greatly preponderant opinion is that proximal ligation, with or without thrombectomy, provides the safest, surest, simplest and cheapest prophylaxis against pulmonary metastasis of the clot.

Regardless of the therapy preferred by the individual physician, however, the selection of cases for treatment rests primarily on the diagnosis of the presence of these thrombi. But establishment of the diagnosis is in itself not at all adequate, the diagnosis must be made at the *earliest possible moment* if the duties of the physician to the patient are to be fully discharged. Welch and Faxon<sup>12</sup> state the problem concisely by asserting that the importance of the diagnosis of deep phlebitis is exactly in reverse ratio to the ease with which it can be made. The surgeon who waits for the full-blown picture of phlebothrombosis, edema of the calf and foot, distended superficial veins, well developed tenderness of the calf and sole, cyanosis of the part, a positive Homans test,<sup>13</sup> a low-grade fever, tachycardia and an increased sedimentation rate will have lost his greatest opportunity to prevent emboli. There of course remain certain patients in whom the first suspicion of venous disease is aroused by an episode of pulmonary embolus. This contingency has been mentioned by Bancroft,<sup>10</sup> by Allen,<sup>14</sup> who states that chest pain was the first sign in 41 per cent of 202 patients, and by Veal and Hussey,<sup>15</sup> who found that in 10 of 84 patients an embolus was the first factor that drew attention to venous occlusion.

It seems reasonable, however, to predict that the incidence of such unexpected emboli will be substantially reduced by daily or twice-daily inspection of the calves and soles in cases in which the patient's age, the nature of the illness or operation and relative immobilization lead one to expect phlebothrombosis. The examination requires only a few minutes, thus imposing a small price for the prevention of the great majority of these tragedies.

It has been stated that the diagnosis must be made extremely early if the patient is to receive the fullest value of the available procedures. Accordingly, the clinical picture described above must be recognized as the advanced phase of the disease, a phase in which probably the greatest hazard has

\*From the Surgical Service, Gallinger Municipal Hospital.

†Chief surgical officer, Gallinger Municipal Hospital.

the stage in which the greatest risk of pulmonary metastases has passed

The limitations of venography in making the early diagnosis are discussed. Evidence is also presented that the other great standby, the Homans test, is fraught with certain unavoidable fallacies that result in a dangerously large number of false-positive and negative responses.

A clinical test for the differentiation of early phlebothrombosis and the lesions simulating it is described, and the results of its clinical trial are outlined.

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## THE REGIONAL INJECTION OF PENICILLIN IN LOCAL INFECTIONS

### A Preliminary Report

DAVID ROSE, M.D.,\* AND DAVID HURWITZ, M.D.†

BOSTON

THE advent of penicillin has opened up innumerable fields of exploration in the treatment of infection. Sufficient work has been done and enough reports have been published on the production, assaying and pharmacology of the drug to permit omission of their discussion. This report is mainly concerned with the administration and dosage of penicillin in local infections, with direct regional injection and without systemic injections or other local therapy.

There have been many attempts to use penicillin locally. Peck<sup>1</sup> reported 15 cases in which this drug was employed locally with good results. He, however, also used it systemically, and in some cases in combination with sulfonamides and local treatment consisting of x-ray and incision. The local use consisted of injection into the necrotic mass or a sinus and prevention of drainage by occlusion with adhesive tape. These treatments were often repeated every three hours, each dose consisting of 100 to 1000 units. Florey<sup>2</sup> recommended the use of penicillin locally. He found it best to establish a closed cavity when possible, into which penicillin could be instilled and from which exudate could if neces-

sary be sucked periodically. Cutler<sup>3</sup> advocated penicillin mixed with dehydrated human plasma and applied with a powder insufflator. Sophian<sup>4</sup> recommended an ointment containing penicillin for topical application for furunculosis and similar infections. Flippen<sup>5</sup> states that penicillin may be injected into a localized abscess cavity after aspiration of pus. He warns against the spread of infection by the purely mechanical means of distending firm areas of cellulitis, which we have proved in our series to be an unnecessary cause for alarm. Poate<sup>6</sup> advocates the use of penicillin in solution, introduced through a fine tube into wounds, and as a powder, which is sprayed. Fisher<sup>7</sup> reported 95 cases treated by instillation and irrigation, in which the lesion was either open or well drained.

The present report is a preliminary one on the use of penicillin by direct injection into the infected tissues. This method is in contradistinction to so-called "injections" that are actually instillations into sinus tracts or cavities, the drug being retained by occlusion of the tract opening by adhesive tape or other means. In this series, the penicillin was injected hypodermically, the size and length of the needle varying with the type and size of lesion treated. The best results were obtained by injecting well outside the involved area and directing the

\*Associate visiting surgeon Cambridge Hospital and senior visiting surgeon, Cahill House, Cambridge City Hospital

†Associate visiting physician Cambridge Hospital

deep veins by a simple test. The test employed is as follows:

Firm pressure of the fingers is used to explore for tenderness in any area of the posterior calf (Fig. 1). When the level of tenderness has thus been deter-

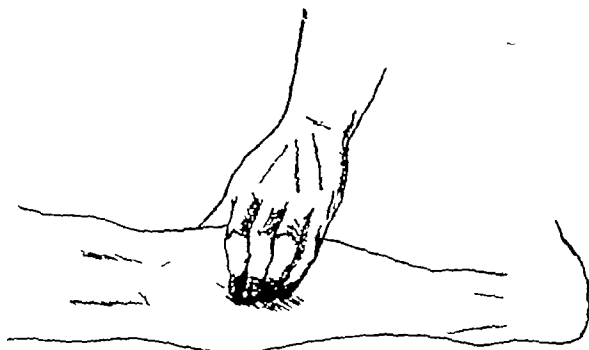


FIGURE 1 The First Maneuver

*This comprises a careful search for tenderness in the deep posterior calf by direct compression with the fingertips in the anteroposterior direction.*

mined, the calf is firmly compressed from side to side, and the degree of tenderness is compared with that elicited in the first part of the test (Fig. 2). In the presence of bland venous thrombi, the skin, subcutaneous tissue, fascia and muscles show little, if

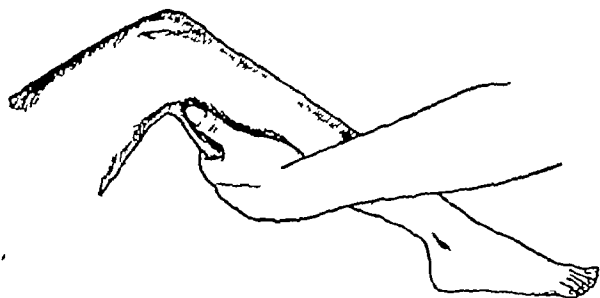


FIGURE 2 The Second Maneuver

*The calf is firmly compressed between the fingers and the palm in a lateral direction. In early phlebothrombosis this lateral compression is painless or relatively so, as compared with the first maneuver. The great majority of lesions simulating incipient thrombosis are accompanied by considerable tenderness on lateral compression. The findings in a case of peripheral neuritis, however, may be similar to those in a case of phlebothrombosis; accordingly, a brief neurologic examination of the extremity is included as the third maneuver.*

any, tenderness on firm compression, whereas direct pressure on the veins, as executed in the first maneuver, causes definite pain. On the other hand, the superficial tissues are extremely tender at the second test if the tenderness resides in their layers. These two stages do not, however, rule out tenderness of the deep calf nerves, such as is present in a peripheral neuritis. The third part of the test is therefore a brief neurologic examination, with a search for al-

terations of cutaneous sensation and an evaluation of position sense of the toes, the vibratory sense and the deep reflexes.

Thus, given a patient in whom tenderness in the calf, either localized or diffuse, is discovered, the suspicion of a deep-vein thrombosis must be entertained. If lateral compression of the belly of the calf at this level is painless or markedly less painful than direct posterior compression, a presumptive diagnosis of phlebothrombosis is indicated. If cutaneous sensation, position sense, vibratory sense and the deep reflexes are then found to be normal, the final diagnosis of phlebothrombosis is warranted.

This test was first used in 12 cases in which thrombi were proved by operative exploration to be present in the venous system of the lower extremity. In each patient the criteria outlined above were exactly satisfied. In 3 cases there was neither pain nor limitation of dorsiflexion on forced passive dorsiflexion of the foot (Homans test). In 2 of 5 patients tested the venogram showed no definite block in either the calf or femoral veins.

Following this experience, proximal venous ligations have been performed at various levels in 59 cases. In 31 of these, phlebothrombosis was diagnosed, the remainder of the ligations being performed for prophylactic purposes, usually in the contralateral legs. In all the 31 cases, in which venous occlusion was suspected, the test described above was positive. In 14 of these, a clot was demonstrated by opening the femoral vein or the iliac vein. Of the remaining 17 cases, there was roentgenologic demonstration of pulmonary emboli and infarctions in 12. Since 95 per cent of pulmonary emboli are known to arise in the leg veins, this is strong presumptive evidence of peripheral phlebothrombosis.

In addition to these cases, I have seen 65 other patients in whom incipient phlebothrombosis was suspected. None of these cases yielded the findings described above, and in none was there subsequent evidence of advancing thrombosis, such as emboli, leg edema, cyanosis, venous distention or progressing tenderness. Twenty-six patients, however, showed calf pain on forced dorsiflexion and 31 presented some degree of limitation of dorsiflexion.

#### SUMMARY

The high incidence of phlebothrombosis of the leg veins is reviewed, and the lethal potentialities of the condition are discussed.

Considerable stress is placed on the early diagnosis of bland venous thrombi so that methods of prevention of pulmonary embolus may be instituted before the occurrence of this dreaded complication. Detection of these thrombi at this stage requires abandonment of the present dependence on finding the classic picture of thrombophlebitis, because this syndrome represents the late phase of the disease,

of the needle and progressing toward the center of the infection. The injection was made deeply in the tissue, not merely subcutaneously, except in cases in which the infection was within the skin, such as furuncles. A sterile needle was used for each injection site.

On the following day the lesion was examined and again injected. The dosage and volume were determined in relation to the progress of abatement of infection, and this procedure was continued until infection was completely controlled. A dry dressing was applied and was changed as needed if any discharge was present.

## RESULTS

This series comprised 2 cases of osteomyelitis of the finger, 6 of felon, 6 of carbuncle, 3 of perianal infections, 6 of cellulitis, with and without abscess, and 2 of furuncle. Table 1 shows the types of infection, complications, dosage and so forth.

A few cases are worthy of discussion as illustrating the treatment and the results obtained.

### Osteomyelitis

**CASE 1** L J, a 36-year-old housewife, was a known diabetic patient who had neglected her treatment for 2 years. Twelve days prior to admission, she sustained a puncture wound of the right middle finger. This became infected and was seen by a local physician, who treated it by hot soaks and later by a small incision on the palmar surface at the tip. The finger became progressively worse, and on February 6, 1945, the patient was admitted to the Cambridge Hospital by one of us (D H), who had originally treated her diabetes. He found the diabetes uncontrolled and undertook its management. The finger was incised under general anesthesia and the pus was evacuated. Sloughing down to the distal phalanx was found. Cultures revealed *Staphylococcus aureus*. X-ray examination revealed osteomyelitis. The systemic use of penicillin, 120,000 units every twenty-four hours in divided doses every three hours, was instituted. This dosage was increased to 150,000 units every twenty-four hours and maintained for 8 days. During that time, the finger became progressively worse. There was a dusky, bluish swelling of the entire finger, with severe, constant pain and moderate discharge of pus. On February 13, two injections of penicillin, each of 15,000 units in 1 cc of solution, were made at the base of the finger on the medial and lateral sides toward the tip of the finger. On the following day, the patient was free of pain for the first time and the color and swelling of the finger had markedly improved. The same dosage and volume were employed daily, with the injections made closer and closer to the tip of the finger, the last three being made directly into the localized area of osteomyelitis. On February 19, 6 days after the local injections, the finger was of normal size and color. Motion was free, there was no pain or tenderness, and the discharge of pus had ceased. X-ray films showed slight improvement in the osteomyelitis. The penicillin was stopped, and on February 24 the patient was discharged. The diabetes was practically controlled. Two weeks later the finger was healed. There was no sequestrum.

This was the first case of any sort in which direct injection of penicillin into a local infection was employed. A subsequent case (Case 2) was treated earlier and more vigorously without systemic penicillin, and as good a result was obtained as in Case 1.

### Felons

Felons need no special discussion, since Table 1 is self-explanatory, but one case merits brief mention.

**CASE 7** E R, a 34-year-old female, was referred with felons of both thumbs. The left thumb, which had been incised and drained 7 days previously, was still painful and swollen and was draining freely. The right thumb was acutely infected and was tender, reddened and swollen. Under intravenous Pentothal Sodium anesthesia both thumbs were cleansed and painted. One hundred thousand units of penicillin was dissolved in 2 cc of saline solution, and 1 cc was injected into the left thumb below the depth of the incision. The remainder of the solution, with a fresh needle, was injected into the right thumb at two puncture sites. On the following day, the right thumb was needled and drainage of pus was obtained. No further treatment was instituted, and both thumbs promptly healed.

### Carbuncles

The carbuncles demonstrated a marked and even spectacular response to direct-injection therapy. None of these cases had incision or even separation of bridges between cavitations. In 1 (Case 9), the carbuncle had been incised and drained a week before the patient reached our hands. It is of interest that this patient received more treatments (seven) with a greater total dosage of penicillin (495,000 units) than did those whose carbuncles had not been incised. In all these cases there was spontaneous evacuation of pus and separation of slough within two to five days after the onset of treatment. In some cases in the early stages of treatment heat was applied in the form of poultices or moist dressings. Later the use of heat was abandoned. All the patients were ambulatory following the first treatment. Two cases deserve explanation.

**CASE 10** H C, a 47-year-old, married woman, was admitted to the Cambridge Hospital on March 28, 1945, after having been seen at home in consultation. There was a carbuncle on the lateroanterior aspect of the neck, overlying the large vessels. Its dome was 7 cm in diameter, with multiple oozing sinus points. The base measured 15 cm in diameter and extended down to the clavicle. The skin was reddened and burnt, with a vesiculation, as a result of too vigorous heat therapy before a physician was called. The temperature on admission was 102.4°F, and the pulse 100. The white-cell count was 15,400 and a culture revealed *Staph. albus*. Four cubic centimeters of penicillin, 20,000 units per cubic centimeter, was injected, with four sites of injection. Fifteen minutes after treatment, the patient was able to move her head and felt much more comfortable. On the following day, the area of redness and edema was markedly decreased and only moderately tender. One cubic centimeter of solution containing 30,000 units of penicillin per cubic centimeter was injected at each of four sites, which approached the center of the carbuncle. On the 3rd day the same dosage was employed, and later that day the slough was lifted out *en masse*. No further treatment was given, and 2 days later the patient was discharged home with a practically dry wound. It was completely healed within 10 days.

In this case, the location, size and poor condition of the surrounding skin was such as to make extensive incision and drainage a risky procedure.

**CASE 11** B M, a 43-year-old man with a carbuncle of the left temple, was being treated by penicillin systemically and heat locally when his case came to our attention. The blood sugar was 111 mg per 100 cc. A blood culture was negative, and a local culture was not obtained because there was no discharging pus but only multiple points heading up. On May 11, 1945, 40,000 units of penicillin was given intramuscularly in divided doses and on May 12, 120,000 units was given. Following this, local treatment was advised and 20,000 units of penicillin in 1 cc of solution was injected at each of four sites. On the following day, there was a soft,

needle toward the center of the infected site, and by outlining the injection zone not by the visible cellulitis but by the zone of tenderness to palpation. The latter is often 0.5 to 1.0 cm. beyond the outermost margin of redness in apparently uninvolved tissue. The rationale of this approach lies in an attempt to augment and reinforce the barrier that the body tissues set up to localize the spread of infection. Injection outside of and through the natural barrier to the center of infection thus aids the body reaction not only in preventing spread of infection but also in combating the infected tissue. This is a highly important phase in the administration of penicillin for regional use. Direct injection into the infected mass, although of value, does not produce so rapid and truly spectacular results as does the method described above. In addition to outlining the zone of tenderness, we have divided the area into three or four sections for injection.

In this series, injections were given once daily and the dosage was worked out for each case by virtue of the type, location and extent of infection. No case received solutions containing less than 15,000 units per cubic centimeter, and some received those containing as much as 60,000 units per cubic centimeter. In relation to dosage, there are two factors for consideration — the total volume and the number of units per cubic centimeter. In the first few cases treated, we hesitantly used solutions containing 15,000 units per cubic centimeter and divided the amount injected into two to four parts, depending on the number of sites. As the work progressed, it was found that the concentration could be increased without untoward results. The volume, however, is definitely limited by the site of infection. For example, in cases of felon or paronychia it is difficult to use a large volume, on the other hand, in cases of carbuncles or cellulitis, where there is considerable fatty and areolar space tissue, large volume can be employed.

Several general observations were made. Injections in fingers and hands are painful. This is apparently due more to the volume injected than to the concentration, since high concentrations in small volume were not much more painful than larger but more dilute volumes. Novocain nerve block was tried with some patients, but they complained as much of the block as they did of the penicillin injection. In 1 case, nitrous oxide and oxygen anesthesia was used to permit a high concentration in a felon. Intravenous Pentothal Sodium was employed in a case of bilateral felon. In all cases, within one to four hours after the initial injection the affected part became almost completely free of pain and could be actively used, and palpable tenderness was minimal. In all cases, the area treated became reddened and later mildly cyanotic, the latter condition persisting long after the infection had cleared up. In most cases desquamation of the skin took place after healing,

but in some it occurred during the healing process. There was no toxic reaction, and no sloughing of tissues.

In many cases in which pus formation had become established, spontaneous evacuation occurred during or after the second treatment. In some cases the pus was completely absorbed without evacuation. This brings up the question of desirability of evacuation of pus by needling or even by incision. During the first few treatments it was thought desirable to maintain a closed system so that the penicillin would be kept in contact with the pathogens and tissues more completely and for a longer period of time. It was also found that in the cases with a collection of pus near the surface it spontaneously evacuated during an injection or shortly thereafter. In some cases the pus was evacuated by needle after the initial treatment. For these reasons, we have not employed incision and drainage, and the lesions have responded just as well to treatment without them. This may seem contrary to one of the basic rules of surgical treatment, namely that evacuation of an enclosed pus pocket is the only correct treatment. Although this has been true up to the present, it now appears possible not only to limit the infection but also to overcome it without deforming incisions and with a marked decrease in disability, pain and length of hospitalization. It must, however, be kept in mind that this treatment does not preclude surgery in some cases. Judgment must be exercised in deciding whether the process of healing may be hastened by evacuation of the pus rather than by absorption. In such a case, evacuation by incision or needling can be done, but only after treatment by injection has abated the acute process and complete localization has been attained. To date, there have been only a few cases in which evacuation was done by needling and only 1 in which it was done by incision, in several cases the lesion had been incised previous to admission to the hospital.

In practically all cases, the systemic use of penicillin or sulfonamide therapy was excluded and no x-ray or other local therapy was employed.

#### METHOD OF USE

Penicillin dissolved in saline solution was prepared in the usual manner, the amount of saline used depending on the type and size of lesion to be treated. In fingers and other areas where loose tissue precluded a large volume, 2 to 4 cc. was used to dissolve 100,000 units of penicillin, thus giving a concentration of 50,000 to 25,000 units per cubic centimeter. The parts were cleansed with soap and water and painted with an aqueous solution or tincture of Zephyran, and zones of tenderness mapped out. Whenever possible, two to four sites of injection were chosen. In all cases, the injection was made by hypodermic needle, starting outside the zone of palpable tenderness, injecting slowly ahead

erythematous edema about the upper face, extending into the eye and cheek of the affected side. Because of this, the local treatment was omitted by the attending physician, and 100,000 units was given systemically. On the following day, there was spontaneous drainage and separation of slough, which was lifted out. There were no further treatments, and 5 days later the lesion was practically healed.

This was the only case in which a local reaction was observed.

### Anal Infections

The only comment that can be made concerning the use of penicillin in anal infections, until a larger number of cases are studied, is that local therapy cleans abscesses preparatory to surgical removal of fistulas. In Case 14, the fistula healed completely internally and externally and no later surgery was necessary.

### Cellulitis

Cellulitis, with or without abscess formation, responds favorably to this mode of therapy. In fact, regional injections are of the utmost importance in limiting and localizing the spread of infection. In our 6 cases, there were 3 that never progressed to abscess formation. One case drained spontaneously, in 1 the pus was evacuated by needling, and had a small superficial incision for drainage. All these infections became localized in one to three days after onset of treatment. One case stands out as an example.

CASE 20 J G, a 41-year-old man, sustained a minor laceration over the palmar surface of the proximal phalanx of the left middle finger. Twenty-four hours later, the finger was twice its normal size, reddened and painful. A physician advised hot soaks and 1 gm of sulfathiazole thrice daily. After 3 days, an attempt to reopen the laceration, which had closed over, was made, but no pus was obtained. The same treatment was continued for 2 weeks, during which time the hand became worse. At the end of 3 weeks, when we saw the hand, there was a hard, brawny cellulitis involving the entire middle finger and the proximal portions of the two adjacent fingers, with a softer edema of the entire dorsum and palm of the hand. The finger was cyanotic and in stiff extension. It was tender and the site of a throbbing pain. There was general malaise but no fever. An immediate injection of 100,000 units of penicillin in 2 cc. of solution was made. The sites elected were lateral and medial to the initial laceration, using 1 cc. for each site and directing the needle deeply to the palmar fascia. On the following day, the palmar surface of the hand was only slightly swollen. The palmar surface of the finger was swollen but soft and nontender and its color was nearer normal. Its dorsal surface was still cyanotic, swollen and tender. This time the injection, with the same dosage and the same concentration, was made from the medial and lateral surfaces toward the dorsum. On the following day, the entire finger was normal in color, although with a soft swelling. There was no pain or tenderness. The palm was free of swelling, but there was a slight amount of soft swelling of the dorsum of the hand. The patient stated that he had had the first night of complete freedom from pain since the onset of infection. The finger was still stiff and could not be flexed. Without further therapy other than hot soaks, all swelling disappeared. Although some inability to flex is still present, slow improvement has continued.

### Furuncles

No comment is needed concerning furuncles, since these are relatively simple infections. They respond well. Usually one injection in the sur-

rounding zone or under the base of the lesion is sufficient for complete relief and healing.

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Cultures of all lesions were made when pus was present. The organisms found were either *Staph aureus* or *Staph albus*, except for Case 14, which showed *Streptococcus haemolyticus*.

The results were extremely gratifying. No deforming surgery was done. Evacuation of pus, when formed, was usually obtained by spontaneous evacuation or needling. There were no cases of sloughing, tissue necrosis or dissemination of infection. The reduction of disability (Table 2) and

TABLE 2 Duration of Disability

DIAGNOSIS	SHORTEST PERIOD days	LONGEST PERIOD days	AVERAGE PERIOD days
Carbuncles	4	14	7
Osteomyelitis	14	32	23
Felon	0	2	2
Cellulitis	0	7	4

rapidity of healing are in favorable contrast to the results of orthodox surgical treatment.

### SUMMARY AND CONCLUSIONS

Penicillin employed by direct injection is of definite value in limiting and overcoming local infections.

Concentrations of penicillin as high as 60,000 units per cubic centimeter may be used without complications. One of the values of direct injection is the ability it gives to produce a high local concentration, which is impossible by systemic use of the drug.

Disability is reduced far below the point reached by any other means of treatment.

There is no deformity such as that frequently following radical surgical incision and drainage.

Pain is quickly relieved — in some cases within one hour, and always within thirty-six hours.

Surgical judgment must be exercised regarding the necessity and proper time for evacuation. Preferably, no evacuation should be performed until complete localization by injection therapy has been carried out, and then only minimal surgery is indicated. Most cases evacuate spontaneously during localization, with freedom from pain.

Injections are painful, and the degree of pain is in direct ratio to the density of tissue and the volume of injection.

Injections once daily are adequate, but they must be maintained until definite subsidence of infection is evident.

The fear of spreading the infection by this treatment has not been substantiated. In part, this is due to the fact that injections are started well outside the center of infection, thus reinforcing the barrier and aiding in localization.



TABLE I Summary of Data

CASE No	AGE	SEX	DIAGNOSIS	ASSOCIATED DISEASE	CONCENTRATION units/cc	VOLUME cc	FREQUENCY OF TREATMENT	TREATMENTS	TOTAL units	OTHER TREATMENT	RESULT
1	36	F	Osteomyelitis of finger	Diabetes	15,000	2	Once daily	7	210,000	Incision and drainage on admission, 125,000 units of penicillin systemically for 10 days, without results treatment of diabetes	Complete healing no sequestrum.
2	40	F	Osteomyelitis of finger	None	30,000	2	Once daily	7	420,000	Incision and drainage 2 weeks before treatment	Complete healing no sequestrum
3	18	F	Felon of finger	None	30,000	1	—	1	30,000	None	Absorption, no drainage.
4	19	F	Felon of finger	None	20,000	1	Once daily	3	60,000	None	Absorption no drainage.
5	21	F	Felon of finger	None	40,000 20,000	2 1	Once daily Once daily	1 1	100,000	Pus evacuated by needle day after first treatment	Complete healing
6	21	F	Felon of finger	None	40,000	2	Once daily	3	240,000	Needling 2nd day, no pus obtained	Complete healing; spontaneous drainage 3rd day
7	34	F	Felon of left thumb	None	50,000	1	—	1	50,000	Incision 7 days before admission	All drainage ceased after treatment, healed
			Felon of right thumb	None	50,000	1	—	1	50,000	Needled day after treatment	Complete healing; drainage of pus following needling.
8	47	M	Carbuncle of neck	None	30,000	3	Once daily	5	450,000	None	Spontaneous sloughing complete healing
9	60	F	Carbuncle of neck	None	15,000 30,000	3 3	Once daily Once daily	3 4	495,000	Incision and drainage before admission	Drainage and absorption complete healing
10	47	F	Carbuncle of neck	None	20,000 30,000	4 2	— Once daily	1 2	200,000	None	Slough lifted out <i>en masse</i> after third treatment complete healing
11	43	M	Carbuncle of left temple	None	20,000	4	—	1	80,000	Systemic penicillin 40,000 and 120,000 units before local treatment, and 100,000 units after local treatment.	Following local treatment, edema and erythema extending into eye and cheek, next day, spontaneous evacuation of slough, with rapid recovery
12	48	M	Carbuncle of neck	None	40,000 25,000	2½ 4	— —	1 1	200,000	60,000 units of penicillin systemically	Spontaneous evacuation 2nd day after treatment, complete healing
13	40	M	Carbuncle of left shoulder	None	40,000 45,000	2½ 4	— Once daily	1 4	820,000	None	Slough partially removed 2nd day, completely removed 5th day complete healing
14	13	F	Perianal abscess	Fistula and diabetes	20,000 40,000 20,000	5 3 5	Once daily Once every 5 days Once every 3 days	7 3 2	1,260,000	Treatment of diabetes	Complete healing of tract internally and externally
15	42	M	Perianal abscess (anterior)	Anterior fistula	10,000	4	Once daily	3	120,000	None	Spontaneous evacuation and healing of abscess
16	36	M	Draining perianal abscess (posterior)	Posterior fistula	12,500	2	—	1	25,000	None	Abscess dry 2 days after treatment
17	29	F	Cellulitis of palm	None	10,000	2	—	1	20,000	None	Absorbed completely, no drainage.
18	29	F	Cellulitis of base of thumb	None	10,000	2	Once daily	4	80,000	None	Absorbed no drainage.
19	21	M	Cellulitis of right knee (foreign body)	Diabetes	20,000	2	Once daily	3	120,000	None	Spontaneous drainage after first treatment
20	41	M	Cellulitis of left middle finger, with tenosynovitis	None	50,000	2	Once daily	2	200,000	Sulfonamide treatment for 2½ weeks before admission	Complete absorption residual stuff finger
21	26	M	Cellulitis with palmar abscess	None	20,000	2	Once daily	2	80,000	Needled for evacuation of pus	Complete healing
22	41	M	Cellulitis with palmar abscess	None	50,000	2	Once daily	3	300,000	Increased for evacuation of pus on 3rd day	Rapid healing
23	18	F	Furuncle of neck	None	20,000	1	—	1	20,000	None	Spontaneous drainage day after treatment
24	18	F	Furuncle of neck	None	40,000	1	—	1	40,000	None	Spontaneous drainage on day of treatment

erythematous edema about the upper face, extending into the eye and cheek of the affected side. Because of this, the local treatment was omitted by the attending physician, and 100,000 units was given systemically. On the following day, there was spontaneous drainage and separation of slough, which was lifted out. There were no further treatments, and 5 days later the lesion was practically healed.

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Cultures of all lesions were made when pus was present. The organisms found were either *Staph aureus* or *Staph albus*, except for Case 14, which showed *Streptococcus haemolyticus*.

The results were extremely gratifying. No deforming surgery was done. Evacuation of pus, when formed, was usually obtained by spontaneous evacuation or needling. There were no cases of sloughing, tissue necrosis or dissemination of infection. The reduction of disability (Table 2) and

TABLE 2 Duration of Disability

DIAGNOSIS	SHORTEST PERIOD days	LONGEST PERIOD days	AVERAGE PERIOD days
Carbuncles	4	14	7
Osteomyelitis	14	32	23
Felon	0	5	2
Cellulitis	0	7	4

rapidity of healing are in favorable contrast to the results of orthodox surgical treatment.

### SUMMARY AND CONCLUSIONS

Penicillin employed by direct injection is of definite value in limiting and overcoming local infections.

Concentrations of penicillin as high as 60,000 units per cubic centimeter may be used without complications. One of the values of direct injection is the ability it gives to produce a high local concentration, which is impossible by systemic use of the drug.

Disability is reduced far below the point reached by any other means of treatment.

There is no deformity such as that frequently following radical surgical incision and drainage.

Pain is quickly relieved — in some cases within one hour, and always within thirty-six hours.

Surgical judgment must be exercised regarding the necessity and proper time for evacuation. Preferably, no evacuation should be performed until complete localization by injection therapy has been carried out, and then only minimal surgery is indicated. Most cases evacuate spontaneously during localization, with freedom from pain.

Injections are painful, and the degree of pain is in direct ratio to the density of tissue and the volume of injection.

Injections once daily are adequate, but they must be maintained until definite subsidence of infection is evident.

The fear of spreading the infection by this treatment has not been substantiated. In part, this is due to the fact that injections are started well outside the center of infection, thus reinforcing the barrier and aiding in localization.

We are indebted to Dr Samuel M Perlmutter and Dr Leo A Blacklow for the data on their patients included in this series

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## SYMPOSIUM ON MEDICAL SOCIOLOGY

### PRACTICAL CONSIDERATIONS IN THE PLANNING AND CONDUCT OF A NATIONAL MEDICAL-CARE PROGRAM\*

EDWARD S ROGERS, M D †

**D**URING the course of the preceding few weeks you have had laid before you an exceptionally well chosen review of facts, attitudes and plans with respect to the problem of medicine and its place in a changing social structure Regardless of the details of the views that you have formulated, there probably are few, if any, of you who will not agree that fundamental changes are in motion

Medicine as a science has been through, and is still in, a most amazing period of progress We need not review the evidence here Similarly, other forces of great moment to the social structure have been through periods of growth Transportation provides a good example Its growth and its new horizons have had far-reaching effects on our way of living It seems just as fallacious to adhere to the concept that the advances in medicine will not have their counterpart in changes in the former patterns of medical practice—our manner of living with respect to the use and distribution of medical services—as it would be to claim that modern transport has not brought and will not continue to bring changes in the country's standards and manner of living

These changes are not "around the corner" They are here today and will be even more so tomorrow Let anyone who doubts this but take the trouble to review the major party programs in the last presidential campaign Advances in social security, you will recall, were not an issue challenged by either, and medical care is recognized as an important part of social security

Regardless of the justifiable pride that we all enjoy in the past achievements of the medical profession, regardless of the high quality of the national health and regardless of the apprehensions that beset many in our ranks and make them shut their eyes, the facts in proof of the imperfections of the

present system of medical services are clear I therefore believe that change is not to be feared but rather to be sought

The facts have been ably pointed out to you in previous lectures, and you know them as facts, but how deeply do you feel them? Some of you may have experienced them at first hand, most of you probably have not You do not see people seriously lacking for medical facilities here The social implications of failures in preventive practice are not readily observed in the laboratory, the clinic or the classroom, although they are of course basic and are in the background You are not exposed to poor medicine in the cloisters of this school, and you are not being prepared to practice it But neither the world nor the Nation begins and ends in Boston with both feet in these buildings, as I used to think

I have sat in the seats you occupy, and, like you, I have been inspired, and I have also been put to sleep I am not stirred by any unusual sense of school patriotism, but I have always been proud to have graduated from these halls, because to have done so has numbered me, as it will you, among men well trained and with a high tradition, from among whom many of the leaders of this profession have risen Never before has the medical profession stood in greater need of sane, clear-thinking leadership, both now and in the years immediately before us, and these years will be the years of your increasing responsibility That is why I say that you know these facts but question how deeply you feel them

I have said that the need is great and that you will have much to do in determining the future I shall attempt to show you why

In the light of your studies and discussions, probably each of you has either formulated or is formulating your own plan, your own concept of the solution of the problem of medical care The many and various patterns of such concepts will reflect a variety of molding forces, such as your awareness of need, your experience, your type of information and interest, your intellectual methods and, by no means the least, your basic prejudices Yes, you

\*This is the ninth and concluding of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March 1945 they were sponsored by the Department of Preventive Medicine and were primarily intended for third-year students. These articles have temporarily replaced the reports "Medical Progress"

†Assistant commissioner for medical administration, New York State Department of Health assistant professor of medicine Albany Medical College.

have them, — all of you, — and you have the most in all probability, when you fail to recognize them

In these respects you do not differ greatly from those in whose hands the delicate buds of the future of medicine lie today. To be sure, most of these men have had from a few to many years of experience, and some of them, thank heaven, are real leaders, rich in their ability to evaluate the forces in their own thinking and to recognize the merit in another's point of view. Many, however, are not so. They have had what should be rich experience, but they take a sort of polaroid point of view toward it and see only the things that are in parallel with their prejudices.

I have mentioned the formulation of a plan. This is essential if we wish to end our present more or less haphazard practices and move effectively toward an objective. I shall, however, be but little concerned with other than the broadest aspects of planning today, because what I have to say will apply equally to any plan. It is essentially this: your plan, my plan, the Surgeon General's plan or the President's plan will be no better than its chances of actually accomplishing its objectives.

Plans that purport to answer one phase or another of the problem of medical care are of frequent occurrence these days, and there are about as many variations as there are groups contributing them. Many of these plans have been in operation over a period of years. Especially is this true in other countries. By and large, however, with the exception of Russia, these programs, like those in operation in this country, fall short either of being comprehensive or of covering the entire population. And, as Dr Goldmann<sup>1</sup> doubtless advised you in his lecture, one must be circumspect in the matter of applying the experiences of other nations, with political and social structures so different from ours, as a pattern for our actions.

In this country one finds rapidly growing movements such as hospital insurance under Blue Cross systems, a large variety of voluntary medical and medical-indemnity insurance schemes for the low-income and certain industrial groups and a small but increasing number of fairly comprehensive hospitalization and medical-care plans for the indigent. But none of them, so far as I am aware, embrace comprehensive provisions for health and preventive services and for the improvement of the quality and distribution of medical services for other than limited segments of the population. Nor have they been developed as a part of a planned master strategy that envisions the way they fit into a total program of medical care.

Even in the area of national planning, it seems to me that there has been either too much opportunism or too little regard for sound basic principles, as in the Wagner-Murray-Dingell Bill of 1944. The hospital-construction bill (S-191) of Senators Hill and Burton, now before Congress, impresses

me as being much more realistic, and although it is not comprehensive in the terms of the whole problem, it nevertheless suggests that its authors have a pretty clear concept of how it would fit as a part of a rational master plan.

Among the comprehensive programs recommended by national organizations, that of the American Public Health Association<sup>2</sup> merits attention because it is clear, comprehensive and comparatively simple. Although it achieves this clarity and simplicity by the expedient of confining itself to a statement of a few objectives and principles applicable to method, it does so, of course, at the cost of begging a great many major problems of detail in technic. I am rather of the opinion that this is wise in national planning at this stage, but from the practical point of view of a person who wants to know exactly what he should do as a physician or an administrator, it is not of much help. We must start somewhere, however, and we must have some common ground of agreement regarding where we want to go. Such a common ground, when clearly stated and properly implemented with principles for our guidance, constitutes a master plan in the sense that I am using the term. Not to have such a plan would be analogous to trying to fight the present war without a master strategy. Yet the present lack of basic master planning and agreement in the war on the medical and health needs of the country is of this order.

You cannot escape your present and increasing responsibility and concern in this problem. You cannot evade it today as citizens. You should not evade it tomorrow as physicians. And some of you, I hope, will assume roles of leadership with respect to it in the years that lie ahead. It is not a problem that will be solved with the mere passage of a bill or two.

Accordingly, I want to discuss with you certain points of view and problems that may serve as guides to your thinking in relation to your responsibilities as citizens, physicians and potential leaders among physicians.

First of all, you should establish a set of values with which to measure this business of planning, and second, you ought to attain some insight concerning the practical problems of accomplishing a plan once it is accepted.

What are the fundamentals of a master plan? I can speak only for myself, of course, but to me it seems that such a plan should embrace the following characteristics. It must be clear as to its objectives, and these must be comprehensive in nature. It must be practical and make provision for the logical steps by which it is to be developed. It must meet the needs of and be acceptable to those whom it most greatly affects. It must contain the substance for authority, responsibility and orderly administration. Lastly, it must be flexible with respect to local situations and future developments.

The foregoing principles, platitudinous-sounding and perhaps overly concise, have not been lightly written. In them I have endeavored to include those elements of a plan that will determine whether or not it is realistic and capable of accomplishment. It will be worth while to consider each of these principles in more detail, both as abstract principles and in the light of current experience.

*The plan must be clear as to its objectives, and these must be comprehensive in nature.* Although we have achieved no single statement of national objectives in a formal sense, we are not far from it, and we can almost check this off as finished. For example, very few people will take serious exception to the objectives for a national medical-care and health program set forth by the American Public Health Association<sup>2</sup> in December, 1944, which read as follows:

1 A national program for medical care should make available to the entire population all essential preventive, diagnostic and curative services.

2 Such a program should insure that the services provided be of the highest standard, and that they be rendered under conditions satisfactory both to the public and to the professions.

3 Such a program should include the constant evaluation of practices and the extension of scientific knowledge.

Compare these with the following seven principles recently announced by the Council on Medical Service of the American Medical Association<sup>3</sup>:

1 Continued expansion of the practice of medicine with full development of approved voluntary hospital, medical, indemnity, industrial and commercial insurance against the costs of medical care.

2 Development of public-health facilities for preventive medicine all over the country.

3 Development of adequate diagnostic facilities everywhere.

4 The use of the voluntary-insurance principle in caring for the indigent and medically indigent.

5 The development of hospital facilities where present facilities are used to the utmost and are still inadequate.

6 The use of federal funds to aid communities in public-health measures, care of the indigent and construction of necessary hospitals, when local communities are unable to finance the projects, but with the retention of local administration.

7 The creation of a unified federal Department of Health, with a secretary in the Cabinet as the head of the department, such secretary to be a qualified physician.

Although I prefer the form of the American Public Health Association's statement, which is natural, since I had a part in its formulation, there are quite a few points of similarity in these two sets of objectives. Of course, those of the American Medical Association are not statements of pure objective, being intermixed with recommendations for the voluntary-insurance principle and other matters of method that are questions of an extremely controversial nature, and by the inclusion of which the framers detract from the force and value of their position.

Returning to the broad topic of social objectives, there is expectation that the President will include in a revised bill of rights, which it is thought he will present to Congress in the near future, as one among

eight or so others, the right to adequate food, clothing, shelter and medical care.<sup>4</sup>

Thus we find evidence of growing acceptance of a new concept — Congress painting in the broadest terms the rights of man, the American Medical Association moving a considerable distance from its former reactionism to admit of similar objectives, but with reluctance to face the realities of their fulfillment, and the American Public Health Association directing its recommendations in a more or less intermediate path, recognizing the merit of the objective but at the same time aware of the difficulties besetting its accomplishment. These, of course, are not the only groups that have made recommendations based on prolonged study,<sup>5-11</sup> but in general these other proposals lie within the limits of the views of these two associations with respect to their objectives.

*The plan must be practical and make provision for the logical steps by which it is to be developed.* By and large, people who study and think about these things at all can be classed in one of four groups.

First, there are the *revolutionists*. I do not mean anarchists, but rather those who believe that mass social changes can be brought about by force of law. These are the persons who believe that the end justifies the means, and that where the processes of growth under our democratic system are slow, changes can be worked out in detail in advance in the minds of a few men and more or less set on the rest of their less informed fellowmen through the process of legislation and centralized administration.

Second, there are the *evolutionists*, the progressives, those who feel strongly the need of change or readjustment but admit the imperfections of the human mind in foreseeing the problems to be faced and in devising their solution other than by a process of trial and error. To this process they add a provision for a positive sort of force pushing things along. These persons like to think of progress as a step-by-step procedure at a reasonably accelerated rate.

Third, there is a group who might be called the *slow evolutionists*, a somewhat more timid folk, sometimes called conservatives. They are too rational and objective in their approach to deny the desirability of progress, yet they are too fearful, either because of their innate nature, because of misgivings or because of personal risks involved in change, to wish to encourage it openly.

Finally, there is a fourth group, who, at the risk of being hackneyed, I can only refer to as the "worry birds," which, as is well known, fly backward because they do not dare to face where they are going but always like to talk about where they have been. This group, in my opinion, is typified by those usually called the *reactionaries*, the ones who state that because we have made creditable progress no further advance is necessary.

No doubt you have already classified your friends

and acquaintances, possibly yourself, in one or the other of these categories. I should regard myself, — quite possibly fallaciously but in any event with much company — as being in the best group — that is, an evolutionist. I am distinctly dedicated to progress but by the very nature of my experience I possess the utmost respect for the problems that beset the path of such progress.

Each of you will inevitably evaluate plans on the basis of the classification in which you really fall, but I urge that by whatever standards you judge a plan, you consider it in the light of whether it provides practical solutions to the over-all needs as you see them and whether you see in it the structure for logical development.

*The plan must meet the needs of and be acceptable to those whom it most greatly affects.* Again, let me remind you that we are discussing planning in terms of the likelihood of its accomplishing its objectives. The plan must therefore be acceptable, first, since lawmaking is involved, to those who are delegated the responsibility for making laws, second, since technical skills are involved, to those most intimately concerned with the provisions for such skills — namely, the medical profession, hospital administrators and ancillary technical workers, and finally, since public support is essential, to the recipients of the service, who are the public.

Broadly speaking, lawmaking falls into several categories of origin. Legislative acts may arise from political expediency in which the legislators either negotiate among themselves for political advantage, frequently of a somewhat subtle nature, or such legislation is conceived and executed through executive or legislative planning independent of actually crystallized public opinion, often as a result of the demands of pressure groups operating as well organized minorities and in self-interest. On the other hand, legislation may arise from the "grass roots," either spontaneously or as a result of leadership functioning within the structure of the truly democratic system and involving the long and arduous road of public education to a point of public recognition and action in behalf of its own best interests.

It is worth taking a few minutes to comment on the influence of pressure groups in the medical field, because this will throw some light on legislative processes and give further emphasis to the need that has been mentioned of a much more vigorous sense of public responsibility on the part of the medical profession. Two examples in my recent experience may serve as illustrations.

The first, although it represents an abortive attempt of a pressure group, is one of serious proportions and may eventually succeed. In the State of New York there are approximately 25,000 licensed doctors of medicine and 400 licensed osteopaths. Beyond this group there are approximately 2000 chiropractors, some of whom have been practicing for many years under what they choose to

term "practice without benefit of law." In something like twenty-three out of the last thirty years, this group has brought pressure for legislation to license chiropractors, and from time to time they have succeeded in the passage of their bill in one or the other branch of the Legislature. This year, although again defeated, they came extremely close to succeeding.

The interesting fact is that here is a relatively small group that, by persistence and an extremely well organized lobby involving elaborate testimonials and highly organized support from a relatively small proportion of the population, threatens to achieve its objective. In my opinion and that of many others, the licensing of this group to diagnose and treat illnesses of all types, with insufficient training and through the use of methods that we consider to be essentially unscientific, would constitute a step backward rather than forward in the state's responsibility for protecting public service. What they cannot achieve on the basis of scientific justification, however, they may perfectly well achieve eventually through the process of attrition, in which they exhaust the patience of the Legislature and in which the large mass of the public is more or less apathetic.

In this connection, it is interesting to note that the State Chapter of the American Federation of Labor threw its weight behind this bill in what appears to be a misguided attempt to bring about improved services for the workers whom they represent. Their attitude was obviously based on what might be regarded as a failure of the medical profession to recognize the painful and disabling effects of minor back injuries sustained in industry. These often do not present signs and symptoms sufficient to permit acceptance under workmen's compensation. Similarly, and not infrequently, I suppose, these patients may have been summarily dealt with at the hands of physicians who have been beset by the problem of malingering. It appears, however, that they have been more sympathetically received by the chiropractor and quite possibly given some relief through his manipulations.

Another example of the activity of pressure groups in the medical field, which was successful, relates to the Emergency Maternity and Infant Care Program, sponsored by the federal government through the United States Children's Bureau. As you may recall, in the early stages of this program considerable controversy arose over the attempts on the part of the Children's Bureau and certain of the states to set standards limiting the provisions of this program to the services of doctors of medicine. It was not long, however, before a small but highly organized lobby, supported primarily, I believe, by the American Osteopathic Association, succeeded in having the authority for such restriction stricken from the powers of the Children's Bureau. This they achieved through

introduction into legislation of phraseology to the effect that the wife of a serviceman must have the privilege of choosing the "practitioner of her choice," provided that state laws were complied with.

Although I do not wish to embark on the controversial subject of the relative merits of the training of osteopaths and doctors of medicine, the important point is that to obtain its objectives this particular group succeeded in defeating measures that were intended to protect the quality of medical care being provided to wives of servicemen. In so doing, they opened the door for inclusion under the provisions of this program of that large variety of practitioners and cultists who we all know are permitted to practice in some states.

With respect to the acceptability of a national medical-care program, there will be certain fundamental differences in the manner in which such a program impinges on the interests of the medical profession on the one hand and of the consumer public on the other. Obviously, the public will show its greatest concern over two questions—first, whether what it regards to be adequate medical services are physically available, and second, whether they are within economic reach. In general, unless medical facilities are totally lacking, it seems that the public is likely to address its primary consideration to the economic aspects—witness the current increase in the public support of voluntary hospitalization-insurance and medical-insurance schemes.

What the public accepts as good for it in terms of quality as well as quantity of care, however, will probably be determined more by a superficial comparison of the facilities in the community with those in other communities of a similar nature than by any expert evaluation of the services actually available. And in the field of preventive medicine, of course, other than in connection with traditional public-health measures, there is a great lack of public understanding.

I recall the surprise of a young lawyer in the Army returning home on leave who occupied the seat beside me on a plane not long ago. We fell to discussing the problem of medical care, and he seemed quite well informed. In common with most people, however, he believed that voluntary health insurance, supplemented by tax-supported care for the indigent, was pretty well on its way and that it left little to be desired. I was pleasantly surprised and encouraged by his change of attitude when I pointed out to him many of the facts that have already been covered in this series of lectures in relation to the inadequacy of facilities, the varying degrees of skill and opportunity to acquire and to maintain skill on the part of men in practice, the general absence of any systematic way of providing consultation services and specialist services other than in the large centers and the fact that the schemes that seemed to him to provide such a complete answer have fallen far short of doing so.

We cannot, however, hope to reach a large number of people with such a direct approach. We must be prepared to accept the fact that it probably will be easier to satisfy the public as it currently, and somewhat superficially, sees its needs than it will be to obtain public support of the type of program that will be in the best interests of the public well-being in the long run.

So far as the medical profession is concerned, acceptance of any sort will be difficult to predict. Consider, for example, the conclusions that we should have been obliged to draw if faced with this question ten years or so ago. We should have had to expect a complete lack of medical acceptance of hospitalization insurance or voluntary medical-indemnity insurance. Both these were formally resisted by the organized profession, but both of them are endorsed by it today. Similarly, at the time of its inception the Emergency Maternity and Infant Care Program was violently resisted by medical societies throughout the country, some of which held out until growing public opinion forced them to reverse their views. In spite of this, the program is now a going concern, widely and not infrequently enthusiastically accepted by physicians who are practicing under it. To be sure, important modifications have contributed to its acceptance, but it still is much different from the form that these groups in their first demands would have had it take.

These experiences lead to the conclusion that perhaps the medical profession is far more socially minded and far more willing to co-operate with logical and well planned steps of a progressive nature than those who have been leading the opposition to change and progress would care to have us suspect. I have proceeded over a period of years in the conviction that this is true, and I am happy to say that my experience has borne it out.

Certainly the average physician is far too intelligent to accept for long the almost childish manner in which the proponents of reactionism have dealt with him. It appears that all that has prevented the physician from penetrating such methods sooner has been the fact that he has been extremely busy and has usually given superficial, transient and often emotional acceptance to such leadership. But when faced with the real issue and the grave necessity of acting in the face of it, I am confident that he will vindicate himself.

I do not wish to be understood as taking the view that there are no grave problems involved and that the practicing physician should not be concerned, or that there is no danger of the introduction of unreasonable practices through the bureaucratic control of medicine. Judging from the patterns of past experience, there is undoubtedly reason for concern, but this danger will be far less, and probably need not materialize at all, if the medical profession will assume a vigorous and constructive role in

guiding the form of the impending changes that are of such importance to it

There seems to be great fear of governmental control over the physician's salary check and of interference between him and his patient in the monetary contract area, as well as apprehension that a system of salaried positions would result in suppression of the physician's individuality and his opportunity to pursue his work with energy and freedom, and that he would be badly paid

My own experience provides a case in point. I have been a salaried employee with the government of the State of New York for almost ten years. I am neither so rich as some of my classmates nor so poor as others. Not once during the ten years of my employment have I felt the slightest impact of a political nature. Although the question of freedom to work as one wishes is probably a matter that resides as much with the individual as with the system, I have found in the conditions of my employment even greater and less restricted opportunity to develop my interests and to expend my energies in directions that I consider to be worthwhile and productive than I encountered during the period of my private practice.

I have never been able to understand the insistence of fellow physicians on the importance of the privilege of negotiating a direct financial arrangement with their patients. I can recall vividly the extreme distaste with which, as a young man opening an office, I discussed the matter of compensation with my first patient. Somehow or other, it did not seem compatible with the whole philosophy that had stemmed from my training and experience up to that time, and I had a haunting feeling that I should pay the patient for the privilege of working on him those skills that, to me, were a matter of such interest and personal satisfaction.

From a somewhat less emotional and perhaps more practical point of view, it certainly seems that the medical profession would do well to look at the economic aspects of medical care from a strictly realistic angle. If we were to assume that the cost of medical care is comprised primarily of physicians' fees, which, of course, it is not, — and that the values in medical service are comparable to a manufactured product in the luxury class, — which they are not, — the medical profession would be justified in insisting on its right to name its price and to control the conditions under which this product is purchased.

But, obviously, we cannot regard any facet of the field of medical service in such a narrow light. The product of the physician is not a luxury, it is a necessity. In committing himself to a life of service in this field, the physician automatically assumes public responsibility, and in a sense, his life is no longer his own so long as he chooses to practice his profession. These things being so, if the economic aspects of medical service are such as to stand in

the way of its complete accessibility to the public, I do not see how the physician can, in good faith, place his personal fears and considerations above changes that will serve the greater need. Even granting that he should do so, and that all of the more than 170,000 physicians in the country were unanimous in their point of view, I do not see how the medical profession could expect, should it come to a battle, that their small voice would carry much weight against the interests of 140,000,000 people.

On the other hand, the public is not competent to judge the extent of its technical needs or to evaluate the quality of service required or being provided. Just as truly as it has the power to control the economic issue, it is powerless to develop and control the quality and equitable distribution of the services it needs. At this point it must enter a partnership with the medical profession. By the force of this very fact, the medical profession faces a great responsibility and is assured an opportunity, if it wants it, to build into any program provisions for the highest standards for service and continued development. Medical acceptance should be given to nothing short of this.

*The plan must contain the substance for authority, responsibility and orderly administration.* This area in planning is almost sure to give rise to great controversy. It is the area in which the medical profession fears that there will be created a dominating bureaucratic or political control, it is the area of potential regimentation, the danger point in what is so frequently and yet ambiguously referred to as "state medicine." It is the zone of fear because the reasons for it and the potential manner of its conduct are so completely misunderstood.

The history of the process of growth from almost any angle, physical or sociologic, reveals the same fundamental patterns from the period of rudimentary beginnings through expansion, in which trial-and-error is the principal controlling force, to eventual development into a system or a series of complex relations that is likely to be cumbersome and confused because of its size and its overlapping and conflicting activities.

At such a stage, organization becomes essential to survival. This has been true of the growth of our cities, our schools, our banking system, our transportation, our industry, our employment. As these have evolved from simple beginnings into more complex structures, certain forms of organization have had to be introduced. This organization is a form of government.

Similar problems of growth have arisen in relation to the distribution of medical services, preventive medical and public-health services and hospital services. The point has been reached at which there is a pressing need for an over-all master plan for the Nation, for the states and for the major subdivisions of the states that will incorporate patterns for the co-ordination and conduct of these services.



in their proper relation to each other and to the other operating forces in the social structure

There is often confusion with respect to the functions of leadership versus those of authority and administration, but these are not synonymous terms. The medical profession outside of government may very well be so intimately and thoroughly concerned with the affairs of practice, teaching and research that it cannot be expected to develop either the skill, the time or the interest to assume responsibility with respect to authority and administration. Although the profession must recognize its limitations in this respect, it should also recognize the importance and the significance of the contribution that can be made by government — because this is the proper function of government.

It is a peculiar anachronism that while we stand staunchly behind our belief in the democratic system and are now fighting for it, many of us simultaneously deprecate and abuse it by our words and attitudes. Why has organized medicine acquired such a violent, almost reflex response to the word "government," as though assuming that government is inevitably evil? Evidently, it is all right for government to be concerned with matters related to other people, but not for it to set its hand in any way on the affairs of medicine.

Pursuing this line of reasoning, we are obliged to conclude that the medical profession must either believe that it is capable of meeting the needs of the future under circumstances that will permit it to act as its own administrative agent and endow itself with the necessary authority or that it does not recognize the need of administrative functions in the manner in which I have described them. I can only assure you that the task of steering the ship of progress through the trials and obstacles that will lie in its charted course are, in this case, not matters of minor consideration. They will require the exercise of rare judgment in trained hands.

The medical profession makes much of its right to lead, and I too believe this, but we can properly raise the question of where this leadership lies or what its value in respect to the problems ahead is. Are we to look for it from the American Medical Association, which has a long record of inaction and negativism with respect to progress in this field? Are we to look for it from groups such as the newly organized Association of American Physicians and Surgeons, which, as you may recall, is attempting to rally physicians under the banner of organized passive resistance to any government-sponsored medical-care program?

The positions of these groups certainly do not constitute auspicious bridgeheads from which to expect to advance in the areas to which we are addressing ourselves. I believe, however, that true leadership from within the medical profession can and will be found, and that in its over-all planning and in developing the mechanics of administration govern-

ment should not be permitted, as an agent of the public interest, to proceed in the absence of such medical leadership.

Not so long ago I attended a meeting of a committee of a major national medical group at which problems arising from some of the existing federal programs in the field of medical care were under consideration. The purpose of this meeting was to establish patterns for so-called "co-ordinated action" between this national group and the controlling federal agency. There was a strong inclination on the part of the practicing physicians present to set up a special committee and to place before the federal agency what would have been little less than a demand that in the future this agency should call regular meetings of the special committee for the purpose of submitting its proposed policies for criticism and review. I am a strong advocate, as should already be clear, of medical co-operation with government and of the increasing influence of the medical profession in the control of medical affairs, but I opposed this suggestion. My opposition was conditioned by the belief that the proposed relation was essentially a negative one, based on the expectation of antagonism, and that although it might succeed in lessening some of the undesirable features of a potentially bureaucratic program, it would miss its real opportunity. In its place, I believed that it would have been better to have advocated a constant, co-operative working relation in which planning was mutually undertaken and in which the physicians were consulted during the formative stages of planning before conclusions had been reached and plans already drawn that would tend to make discussion become criticism and co-operative effort more or less futile.

It seems evident that no plan can succeed that does not embrace provisions for authoritative control and skillful administration. This I believe to be the function of good government. But equally I believe that good government must provide for the influences of effective guidance and leadership on the part of those who have the most to contribute. In the problem under discussion this would mean medical guidance and leadership.

*The plan must be flexible with respect to local situations and future developments.* This final principle is primarily a philosophy of planning, but it is also a test of the sincerity of purpose of the persons developing the plan. The plan at the national level, it seems to me, must be so fundamental and restrained in its approach to detail that flexibility will not constitute a problem. It is at the state and local levels, where working plans must be devised within the broad national pattern, that planned flexibility becomes a requisite.

Let me illustrate. A given state may start out with an attempt to set up a pattern of medical and health centers based on the health-center concept. Well and good. But supposing it en-

courages a group of hospitals to avail themselves of federal grants and postwar construction funds, only to find that it has gone ahead too rapidly and developed the centers in poor localities or in areas where they are not required. The state would then be confronted with a frozen front involving large investments of public funds and equally large and immovable investments in local public interest. The state program in such an instance would suffer from poor planning and inflexibility. On the other hand if the plan had developed its physical system in the wake of rather than ahead of its services, or at least a reasonably accurate concept of the details of such services, it would have retained flexibility during a critical period. Moreover, the services, not the brickwork, would remain the focal point — obviously a situation more favorable to such changes as the future might necessitate.

I have somewhat the same concern with respect to the potential rigidity of voluntary hospital and other insurance plans. Good as they may now seem, they are not the answer to the total problem and they may become obstacles rather than aids to further progress unless their limitations are clearly recognized by those sponsoring and controlling them. Although such insurance plans may help to meet the costs of medical care, they will do little to improve its quality or to bring about a better distribution of special skills and facilities. Also, they may divert public enthusiasm from the more fundamental issues because they are a sort of halfway measure in the right general direction. Once they are well under way, with large investments and a large following, they may well stand in the way of rather than assist further progress unless open-mindedness and an unusual degree of social consciousness are written into the substance of their charters.

The need for flexibility will run through many other aspects of planning that embrace experimental or temporary expedients. For example, it will probably be necessary, strictly as a matter of acceptability, to employ a fee-for-service basis for compensating physicians at the outset. Yet experience has clearly demonstrated that this is not the best solution, and room should be left for further changes as opportunity may present and experience may justify.

As has already been stated, flexibility in planning is almost an abstract quality — a matter of vision and sincerity. Yet no plan will be realistic that lacks it.

\* \* \*

In preparing the material for this discussion I had both a purpose and a hope in mind. My purpose was to try to give you a glimpse of the problems surrounding the field of medical care as seen through the eyes of a physician in government — in the specialty of medical administration, if you will permit me to call it such.

My hope was simple and not too visionary. I hoped, and still hope that you — or at least some of you — will carry this discussion much farther in your own minds and that it may prove of assistance to you in the continued development of your interest in the medical needs of the Nation. And I hope that you will be ready to carry your share in assuring that whatever steps are taken shall be forward steps.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32091

#### PRESENTATION OF CASE

An eighteen-year-old boy was admitted to the hospital complaining of pain in the left arm.

Four months before admission, while roller skating, he fell, experiencing a sensation of something snapping in the left back under the scapula, this being accompanied by pain. On arising, he was unable to use the left arm because of pain in the shoulder. This pain was aggravated by coughing and radiated to the anterior chest. During the next two weeks, the shoulder pain subsided and he recovered full use of the arm, the chest pain, however, was still present when he coughed. Three weeks before admission he first noticed prominent veins in the upper portion of the left arm. At the same time a constant dull ache appeared along the posterior portion of the left upper arm and became progressively severer. Ten days before admission he was examined by his draft board and advised to go to a hospital immediately.

Two and a half years before admission the patient had migratory joint pains, as well as a red rash on the anterior aspect of both legs. A cardiac murmur was heard at that time but later disappeared. He had had scarlet fever at the age of four years.

Physical examination revealed a well developed and well nourished boy in no acute discomfort. The pupils were regular and equal and reacted to light and accommodation. The thyroid gland was not palpable. The trachea was in the midline. In the left anterior triangle of the neck was a firm mass about 2 cm in diameter, which was continuous with a larger mass in the left supraclavicular fossa near the midline, the larger mass was firm, nontender and irregular. A systolic bruit was heard over an area including the larger mass and the left clavicle. There was dullness to percussion over the apex of the left lung, more marked posteriorly. The breath sounds were absent in this area, with decreased tactile fremitus, otherwise the lungs were clear. The heart was negative. Discrete hard nodes about 5 mm in diameter were palpated in the left axillary region. The abdomen was negative. The left hand

was cold and blue. The biceps and triceps reflexes could not be elicited on either side.

The temperature was 98.6°F, the pulse 80, and the respirations 20. The blood pressure on the right was 120 systolic, 80 diastolic, and on the left, 116 systolic, 90 diastolic.

The red-cell count was 4,700,000, with 15 gm of hemoglobin. The white-cell count was 11,100, with 67 per cent neutrophils. The urine and stools were normal. An x-ray film of the chest revealed a soft-tissue mass measuring 8 by 6 cm in the left upper chest. It was slightly lobulated and continuous with the lateral chest. The remainder of the lung fields was clear. The heart, aorta and diaphragmatic shadows were not remarkable. The first rib on the left was not clearly visualized in its anterior two thirds, but there was a fracture at the junction of the middle and posterior thirds, the second rib on that side was not remarkable. Pulsation of the mass was not noted fluoroscopically.

An operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. CLIFFORD C FRANSEEN: May we see the x-ray films?

DR. MILFORD D SCHULZ: A soft-tissue mass lies in the apex of the left chest laterally and anteriorly. The anterior and lateral portion of the first rib is destroyed (Fig 1).

DR. FRANSEEN: Where is the fracture?

DR. SCHULZ: I cannot see the fracture. The mass appears to be outside the lung.

DR. FRANSEEN: The age of the patient is of primary importance in any bone tumor. I shall discuss this point later. Another important bit of evidence is the fact that he fell and had a snapping pain in the left scapular region. That pain could have been due to a pathologic fracture of the first rib. If there was a fracture, as was interpreted, the pain later eased up some but was still present when he coughed. The next episode was three weeks before admission when he first noticed prominent veins in the upper portion of the left arm, with an ache posteriorly. All this was undoubtedly due to the position and size of the tumor, pressure on the subclavian vein causing the prominent veins. The earlier findings of migratory joint pains and a cardiac murmur apparently have no relation with the present problem.

So far as the physical examination goes, the important thing is the 2-cm mass that was continuous with a larger mass in the left supraclavicular fossa. The fact that it was continuous is perhaps important because we are interested in knowing whether this was a tumor that had metastasized or a primary tumor that had extended in this region, this one point alone may be significant in the differential diagnosis. A systolic bruit was heard over the mass, which can be accounted for on the basis of pressure on the vessels, particularly on the subclavian artery.

Nodes 5 mm in diameter were found in the left axillary region, one cannot put much importance on nodes of this size in the axilla. The arm reflexes could not be elicited, undoubtedly because of pressure on the brachial plexus.

This seems clearly to have been a tumor. What organ did it originate in? We can exclude the lung

involvement of bone usually comes after the disease has been progressive for a year or two, and then not by direct extension, as this must have been. Still other extraosseous tumors that could have invaded the bone are the lymphangiomas and the hemangiomas, but they do not seem likely. There is nothing to suggest a tumor of neurogenic origin. The



FIGURE 1

by the x-ray interpretation. Could it have arisen in the pleura? The tumors that might come from the pleura in this region are the endotheliomas and the sarcomas. They are frequently associated with effusion, which was not present here. Was this something outside the bone invading it secondarily or was it primary in the bone? Could it have originated in the lymph nodes and then have invaded the bone? The first thing to think of at this age is Hodgkin's disease. We know that such a tumor frequently invades bone, but to me this is not the picture of Hodgkin's disease. Hodgkin's in-

neurologic signs here can be interpreted on the basis of pressure. One cannot entirely exclude fibrosarcoma, except to some extent on the appearance of the x-ray films, it is conceivable but unlikely.

If we consider this to be a lesion originating in the bone we must ask, as Dr Channing Simmons has taught us, Was it infectious? Was it metabolic? Was it neoplastic?

There is not much about the appearance of the mass or the systemic reaction to suggest that it was infectious — pyogenic, tuberculous or syphilitic. No serologic test is reported, but it is safe to say

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superspecialization if I were called on to choose a surgeon to operate in such a case, I should not know whom to call, because the tumor involved the chest, the neck and all sorts of organs that are unfamiliar to most of us in the ordinary routine run of surgical practice

I made an incision over the clavicle and resected the medial two thirds of that bone. That exposed the subclavian vessels, which were flattened and compressed to such an extent that it was difficult to see how any blood could get through either the vein or the artery. The tumor arose in the first rib and seemed to involve the second rib, although we thought that perhaps the second rib was merely pressed on by the tumor. For a long time I was uncertain whether to remove it, but ultimately got so far that I had to take it out. This involved tying the thoracic duct and removing long segments of the subclavian and axillary arteries, including the main collateral vessels and one or two others. In so doing, I thought that we would produce a permanent disability to the patient's arm, but since we were dealing with a malignant tumor, this had to be done. We forcibly retracted the brachial plexus. On opening the chest I discovered that the tumor had invaded a portion of the upper lobe of the left lung, and this part of the lung was removed. When we got down to the point where I thought that I had dissected away most of the tumor, I observed what appeared to be invasion of the scalene muscles beyond where I could trace it. So I took out a tremendous mass of tissue including a tumor twice the size of what it appeared to be by x-ray, along with the piece of lung and the large sections of artery and vein. We could look into the patient's chest and see the heart and diaphragm from above. In order to improve the collateral circulation to the arm, I did a sympathectomy, removing the second and third dorsal ganglions.

The amazing thing is that following operation the patient had no trouble with the arm, although it was slightly weak, he used it well.

#### CLINICAL DIAGNOSIS

Chondrosarcoma of rib

#### DR FRANSEEN'S DIAGNOSIS

Chondrosarcoma of rib

#### ANATOMICAL DIAGNOSIS

Ewing's sarcoma of first rib, with extension into mediastinum, lung and neck

#### PATHOLOGICAL DISCUSSION

DR CASTLEMAN The gross appearance was that of a meaty tumor, not the gelatinous type that one sees in a chondrosarcoma. There was tumor at the resected edge where Dr Sweet had cut across, and histologic examination showed a rapidly growing

Ewing's tumor. Following operation the patient received x-ray treatment with the million-volt machine. He may do well for a while, although I do not know of any cures of Ewing's tumor except one that Dr Schulz told me about yesterday.

DR SCHULZ In 1939, at the Huntington Hospital, a boy, then five years old, was seen in whom we discovered, more or less by accident, a tumor involving the right eighth rib. The lesion was biopsied, and sections were sent to quite a number of pathologists, who made the diagnosis of Ewing's tumor. X-ray treatment with the Huntington Hospital's million-volt machine was given, and he has been well since. This is one of the rare cases of Ewing's tumor in which the victim has survived for more than five years.

DR CASTLEMAN The tumor was not removed?

DR SCHULZ No.

DR FRANSEEN It would be interesting to know whether the mass in the anterior triangle was a mediastinal node that had become continuous or was part of the main tumor.

DR CASTLEMAN No lymph nodes were involved. The tumor in the neck was an extension of the primary lesion.

### CASE 32092

#### PRESENTATION OF CASE

A fifteen-year-old girl was admitted to the hospital complaining of swelling of the face and legs.

One year before admission, following an upper respiratory infection, edema of the face, hands and ankles appeared, associated with dyspnea and orthopnea. There was no oliguria or hematuria. At another hospital the blood pressure was found to be 145 systolic 100 diastolic. An intravenous pyelogram revealed normal calyces, pelvis and ureter on the left, there was no function on the right. A retrograde pyelogram revealed a small contracted right kidney, with normal calyces, pelvis and ureter. No calculi were found. While the patient was in the hospital, the blood pressure varied from 140 systolic, 90 diastolic, to 170 systolic, 40 diastolic. The nonprotein nitrogen varied from 36 to 49 mg per 100 cc, and the serum protein from 3.6 to 4.3 gm. Albuminuria was constantly present. At the time of discharge, she was free of edema and felt well. She remained well until two weeks before admission, when, with the development of an upper respiratory infection, the same symptoms reappeared, accompanied by pain in the abdomen and in the costo-vertebral angles. There were no urinary symptoms. She felt fatigued, and a cough with tenacious sputum developed.

The past history was noncontributory. She had not had scarlet fever.

Physical examination revealed a well developed

that it was done, because it is almost an invariable rule in any case of bone tumor to rule out syphilis, which can simulate most of these lesions. Another condition that comes to my mind, because I was caught on it three years ago, is an eosinophilic granuloma of the rib. That condition, however, shows a somewhat punched-out area in the rib, and I know of no case in which a tumor mass has been produced. Thus, there is nothing in this case to suggest an infection, nor is there anything to suggest a metabolic disturbance.

So we come to the fact that it must have been neoplastic. Was it benign or malignant? The regular contour suggests a benign lesion. Was it metastatic or primary? The metastatic lesions that occur at this age are few. Ewing's tumor can metastasize to a rib, the other metastatic lesions that occur in children, such as the neuroblastomas, usually appear at an earlier age, and there is no clinical or other evidence to suggest that metastases had occurred.

This then appears to have been a primary tumor, and the differential diagnosis lies between myeloma, Ewing's tumor and osteogenic sarcoma. We can discard myeloma because the great majority of them occur in patients over forty and the tumors are usually multiple. The only thing that suggests it is the pathologic fracture, because statistically 50 per cent of cases of myeloma have pathologic fractures at some time during their course, frequently in the rib. In this case I believe that we can exclude it on the basis of age alone.

How about Ewing's tumor? Ewing's tumor originates in the spongiosa of the bone and is not a cortical destructive lesion, therefore not many pathologic fractures occur with it. Another possible reason for the absence of fractures in Ewing's tumor is that pain is so prominent that the bone is protected, particularly the long bones.

When osteogenic sarcoma does occur in the rib, it is usually the sclerosing type, but the chondroblastic type is likelier to have pathologic fractures because of the bone-destructive effect.

So I have narrowed the diagnosis down to osteogenic sarcoma, with its variations, and Ewing's tumor. This patient was eighteen years old, an age group in which both these tumors occur, in Ewing's tumor 95 per cent of the patients are below twenty-five years of age. This site is rare in both tumors, although both do occur there. I have never seen a Ewing's tumor of the rib in this country, but I did see three in quick succession in Sweden — all rare diseases seem to come in groups of three.

The other thing to be considered in the differential diagnosis of this case is the presence or absence of metastases. Was the tumor mass in the anterior triangle of the neck a metastasis or was it continuous with the primary tumor? This is quite a long way for a tumor of the rib to extend, but it would be likelier in a case of Ewing's tumor than in one of osteogenic sarcoma. Metastases in osteo-

genic sarcoma are extremely rare. I have only seen two such cases — one a paravertebral metastasis and the other a case in which there were bone-forming metastases in the axilla. It does occur, however, as I have said, more commonly in Ewing's tumor than in osteogenic sarcoma. Ewing's tumor, as you know, is usually accompanied by a febrile reaction. This patient was in good general condition on physical examination. On a statistical basis, two thirds of all malignant tumors of bone are osteogenic sarcoma. If this was osteogenic sarcoma, what is the likelihood of the sclerosing form? Osteogenic sarcoma in the rib is usually sclerosing, but there is not much about the x-ray picture to suggest that this was a sclerosing type of tumor. The other form is chondrosarcoma or chondromyxosarcoma. From the evidence we have, I favor a primary tumor of the costal cartilage of the right first rib — a chondrosarcoma, possibly with myxomatous elements. As you know, such tumors invade along the rib, which makes it necessary to remove the entire rib. In any case, one should not be satisfied in removing the tumor alone, if possible, the entire rib should be removed.

DR BENJAMIN CASTLEMAN Dr Richardson, have you any comment?

DR WYMAN RICHARDSON This patient was on the medical service for a short time and I made a diagnosis of malignant tumor and yelled for Dr Simmons.

DR CASTLEMAN Dr Berg, you also saw this patient.

DR ROBERT L. BERG Dr Helen Pittman saw him on the first day and thought that a block resection should be done immediately because of the possibility of rapid extension. I think that we were all agreed on the diagnosis of malignant tumor, but like Dr Richardson, no one tried to be more specific.

DR RICHARD H. SWEET My point of view was much like that of Drs Franseen, Richardson, Pittman and Berg. It was obviously a malignant tumor. I made a preoperative diagnosis of chondrosarcoma, which is, in my experience, by far the most frequent primary malignant tumor of rib, as Dr Franseen has said, excluding multiple myeloma. Although he has not seen any cases of Ewing's tumor of rib in this country, I saw one case some years ago, but I still regard it as a rather unusual occurrence. These were the two tumors considered in differential diagnosis.

From the clinical aspect of the case it was obvious that we were dealing with a malignant tumor and that the prognosis was bad. But it seemed to me that, with a young boy of eighteen in a remarkably good state of health, we should make an attempt to remove the tumor. It so happened that the first-year anatomy class was watching the operation from overhead, and it turned out to be a remarkable lesson in anatomy. In these days of

before the final admission. It would be interesting to know whether albuminuria or hypertension persisted throughout the long asymptomatic interval. Two weeks before admission she again became ill, went downhill quickly in the hospital, and died six weeks after the return of symptoms.

The terminal uremia was typical of that seen in chronic glomerulonephritis, as well as in other types of chronic Bright's disease. Severe renal failure was shown by the low fixed specific gravity of the urine, the greatly diminished or absent excretion of dye in the renal-function test and following intravenous pyelography respectively, the markedly elevated nonprotein nitrogen, the lowered serum calcium, the elevated phosphorus and the lowered carbon dioxide content. The serum sodium and chloride values were within normal limits. The moderate anemia is a frequent finding in uremia.

Like the earlier episode, the onset of this illness, apparently an acute exacerbation of a chronic glomerulonephritis, accompanied an upper respiratory infection. She had a cough and raised some sputum, which showed Type 22 pneumococci on culture. The pleural fluid obscured both the physical and x-ray examinations and made it difficult to be certain whether or not these organisms were associated with a pneumonic process. The normal temperature and the only slightly elevated white-cell count suggest that no significant pulmonary infection was present.

Again, edema of the eyelids and face was a striking feature of the clinical picture, and the serum protein was somewhat low. Part of the generalized edema was due to cardiac failure, which will be considered later, but much of it was of the nephrotic type, a common feature of chronic glomerulonephritis. The patient had pain in the abdomen and costovertebral angles, which is often seen with an exacerbation of a chronic process of this sort.

The urinary findings are of interest. Albumin and white cells were found, although, despite the severe degree of renal damage that was present, no red cells or casts were seen. Presumably the marked pathologic changes in the kidneys in this terminal stage prevented the excretion of these elements.

Congestive heart failure, so often seen in chronic glomerulonephritis, was manifested in this patient by dyspnea, orthopnea, dependent edema, bilateral pleural effusions, enlarged hilar shadows, ascites, a gallop rhythm and an enlarged tender liver. The heart size could not be definitely determined by physical or by x-ray examination. Liver function as tested by the cephalin-flocculation test, the prothrombin time and the van den Bergh reaction, was normal. Digitalis and Mercupurin gave some

diuresis, but death occurred due to a combination of uremia and cardiac failure.

#### CLINICAL DIAGNOSES

Chronic glomerulonephritis  
Uremia  
Cardiac failure

#### DR LINENTHAL'S DIAGNOSES

Chronic glomerulonephritis, with uremia  
Congestive heart failure  
Congenital hypoplasia of right kidney

#### ANATOMICAL DIAGNOSES

Chronic glomerulonephritis of left kidney  
Congenital hypoplasia of right kidney  
Congenital malformation of left kidney  
Cardiac hypertrophy, hypertensive type  
Pericarditis, uremic  
Anasarca  
Bronchopneumonia

#### PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY: Dr Linenthal has accurately predicted the pathological findings in the kidney. The right kidney was extremely small, weighing only 10 gm. The pelvis was quite normally developed, but the renal parenchyma consisted only of a shell 2 mm in width in which no structural detail, such as differentiation into cortex and medulla, could be observed. Microscopically the sections showed only a single glomerulus and a mass of undifferentiated tubules filled with dense colloid casts. Except for a slight pyelitis there was no evidence of inflammation, and the picture is that of a congenitally hypoplastic kidney. The left kidney was also markedly abnormal in development, consisting of two almost separated lobes. It weighed 95 gm. The capsule stripped with difficulty and left a finely granular surface. Microscopical examination revealed great destruction of the glomeruli, widespread interstitial fibrosis and marked dilatation of the persisting tubules. The blood vessels showed extensive secondary sclerotic changes. There was no evidence of acute progressive glomerulitis. The chronicity of the process answers Dr Linenthal's question about the first admission. It seems quite certain that she must have already had a chronic process at that time.

The other findings at autopsy were such as might be expected in a case of chronic nephritis. There was a terminal fibrinous pericarditis, and the heart was slightly hypertrophied. The lungs showed edema and focal pneumonia. There was generalized edema.



and well nourished girl who was dyspneic and orthopneic and had a hacking cough productive of yellow, mucoid sputum. She was not cyanotic or jaundiced. The skin was pale. The eyelids and face were edematous. The tongue was dry and coated. A few small cervical lymph nodes were palpable. The heart was questionably enlarged to the left. There were no thrills or murmurs. Dullness to percussion, diminished breath sounds and moist rales were found over the right base posteriorly. The abdomen was diffusely tender, so that palpation was unsatisfactory. The liver edge was tender and palpable three finger-breadths below the right costal margin. Tenderness was also elicited over both costovertebral angles. The sacrum and lower extremities were markedly edematous.

The temperature was 98.6°F, the pulse 70, and the respirations 20. The blood pressure was 145 systolic, 114 diastolic.

The red-cell count was 3,500,000, with 10.2 gm of hemoglobin. The white-cell count was 10,700, with 74 per cent neutrophils. The urine was cloudy and yellow, with a specific gravity of 1.008. It gave a +++ test for albumin, and the sediment contained 50 to 60 white cells per high-power field, there were no red cells or casts. The Sulkowitch test for urinary calcium was negative. The non-protein nitrogen was 125 mg per 100 cc. The serum protein was 5.3 gm per 100 cc, with 3.1 gm of albumin and 2.2 gm of globulin. The serum cholesterol was 164 mg per 100 cc, the sodium 138.8 milliequiv and the chloride 99 milliequiv per liter, and the calcium 7.6 mg and the phosphorus 6.5 mg per 100 cc. The prothrombin time was 27 seconds (normal, 18 seconds). A cephalin-flocculation test was negative in twenty-four and forty-eight hours. The van den Bergh reaction was normal. A blood Hinton test was negative. A throat culture was negative for beta-hemolytic streptococci. A sputum culture showed rare beta-hemolytic streptococci and a moderate number of Type 22 pneumococci. The urine was sterile.

A chest plate showed a considerable amount of pleural effusion bilaterally. The hilar shadows were quite prominent, but the lung fields were obscured in their lower half by the fluid. The heart shadow was not clearly outlined because of the adjoining density in the chest.

The patient was digitalized. She vomited occasionally. An electrocardiogram taken on the fifth hospital day showed sinus arrhythmia, with a rate of 100. QRS<sub>1</sub> was upright and low, T<sub>1</sub> flat, and QRS<sub>2</sub> slurred. The PR interval was 0.18 second. T<sub>2</sub> was low upright, QRS<sub>2</sub> slurred, T<sub>2</sub> slightly inverted, S prominent in CF<sub>1</sub>, T flat in CF<sub>1</sub>, and T low and upright in CF<sub>2</sub> and CF<sub>3</sub>. Two days later a concentration test of renal function showed fixation of specific gravity at 1.006. A phenolsulfonephthalein test showed less than 10 per cent total excretion in two hours. The serum carbon dioxide content was

15.8 milliequiv per liter, and at that time the non-protein nitrogen was 50 mg per 100 cc. An intravenous pyelogram taken on the tenth hospital day showed extremely poor detail because of the large amount of fluid in the abdominal cavity. There was a small amount of gas in several loops of small intestine, without distention. The kidney shadows were not clearly outlined. Over a period of sixty minutes no dye was excreted by either kidney. The urinary passages were not outlined. Fair diuresis was obtained with Mercupurin, but nausea and vomiting persisted, the latter becoming projectile in nature.

On the nineteenth day the nonprotein nitrogen rose to 160 mg per 100 cc. The patient became unresponsive. A gallop cardiac rhythm appeared. She expired on the twenty-ninth hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR ARTHUR J. LINENTHAL. This patient had renal disease, as manifested in the clinical picture of the illness one year before admission and in the final episode, which was terminated by a combination of renal and cardiac failure. The problem is to determine the nature of the renal lesion.

The nephrotic picture of the disease, as evidenced by marked generalized edema, suggests glomerulonephritis rather than pyelonephritis or nephrosclerosis. In addition, the youth of the patient is against a primary vascular disease, and at no time was there evidence of urinary-tract infection. The edema and marked albuminuria raise the possibility of a degenerative disease of the tubules, that is, nephrosis, but the elevated blood pressure, evidence of renal failure and normal serum cholesterol are against this diagnosis. The pyelographic demonstration of a small contracted nonfunctioning right kidney is of interest, but the absence of obstruction or infection and the normal calyces, pelvis and ureter suggest that this kidney was congenitally hypoplastic and that this anomaly was unrelated to the renal disease, although the kidney was probably involved in the inflammatory process, which is typically bilateral.

In attempting to explain this patient's illness on the basis of glomerulonephritis, the question arises whether the episode one year before the final admission represented an acute process or an exacerbation of a chronic stage of this disease. The absence of hematuria is somewhat puzzling in either case. The relation to an upper respiratory infection and the edema, dyspnea, orthopnea, elevated blood pressure, albuminuria and slightly elevated nonprotein nitrogen are of little differential value. Aside from the rather low serum protein, which suggests a chronic process, there is nothing further to aid in the differentiation.

We are not told the duration of this first period of illness, but the patient recovered completely so far as symptoms are concerned and was well until shortly

elsewhere in this issue of the *Journal*, aggressive attempts should be made to publicize these facts among physicians, as well as among diabetic patients

More reports of the results of treatment in series of coma cases are needed to emphasize the serious prognosis in diabetic coma, especially in patients with unconsciousness and with complications. Laboratory facilities should be more generally available to all doctors for emergency determinations of the blood constituents, as aids both in diagnosis and in treatment. Prompt diagnosis and aggressive treatment in the early stages have been shown not only to relieve the acidosis but also greatly to enhance the patient's chance of recovery from an otherwise severe or fatal complication

### THE COMMITTEE ON GROWTH

IN THE past, the control and treatment of cancer has been attacked by many able men the world over, and it is unnecessary to point out that many notable advances have been made. It is true, however, that the problem of malignant neoplastic disease, which in essence is that of ceaseless, profitless and often uncontrollable growth, has been approached by individual groups of men with rather specialized training and abilities. There have been the pathologists, like the late Drs Mallory and Ewing, who defined and delineated groups of cancer, there have been the clinicians, who have studied the natural history of the disease and have worked out helpful and even curative surgical measures, there have been the radiologists and physicists, who have greatly advanced the technical weapons with which cancer may be attacked, there have been the geneticists, the biologists and the chemists, who have enriched knowledge of hereditary factors and carcinogenic agents, and there have been the public-health officials, who, through appropriate and legitimate propaganda, have educated the public to seek medical advice earlier and to accept more readily the available hospital facilities. But when all is said and done, it must be admitted that, as a general thing, these men, however able, worked in comparative isolation, each pursuing the line of investigation to which he was most suited and for

which he was best trained. This is not to say that their contributions were not of the first order — they were. The tactics were excellent, but the overall strategy was perhaps lacking or at best in the background.

As has been said, the essence of the problem is that of ceaseless, profitless and often uncontrollable growth. It is therefore gratifying that there has been created within the Division of Medical Sciences, National Research Council, the Committee on Growth, which as a body will function as a scientific adviser to the American Cancer Society. This committee is a true board of strategy, an integrating body composed of the foremost men in their respective fields. By their general direction and with their combined and unified help it may properly be hoped that the solution of the cancer problem is nearer at hand. Under a general staff headed by Dr Cornelius P Rhoads and including such outstanding scholars as Drs Dochez, Hastings, Sabin, Little and Winternitz, there are divisions of biology, chemistry, clinical investigation and physics. Within these divisions are panels covering such diverse departments as radiology, endocrinology, nutrition, enzymes, mutation and botany. Each of these panels, in turn, is headed and staffed by outstanding investigators, such as Drs Cowdry, Dubos, Albright and Castle. Presumably it is the intent of this excellent committee to integrate the existing investigations in the field of cancer and to initiate new ones. If such be the case, — and there is every reason to believe that it is, — the future of cancer investigation is bright indeed.

### MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

#### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Lowell	March 1	Albert H Brewster
Salem	March 4	Paul W Hugenberger
Haverhill	March 6	William T Green
Brockton	March 14	George W Van Gorder
Worcester	March 15	John W O Meara
Pittsfield	March 18	Frank A Slowick
Springfield	March 19	Garry deN Hough Jr
Fall River	March 25	David S Grice
Hyannis	March 26	Paul L Norton

Physicians referring new patients to clinics should get in touch with their district health officers to make appointments

# The New England Journal of Medicine

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## EARLY DIAGNOSIS AND TREATMENT OF DIABETIC COMA

DURING the seventy years that have elapsed since the discovery of the ferric chloride test for diacetic acid in the urine, intensive study of ketosis as it occurs both in diabetes and in nondiabetic states has greatly increased knowledge concerning its relation to the metabolism of carbohydrate, protein and fat

In diabetic coma the essential disturbance in carbohydrate metabolism is due to the relative or absolute lack of insulin. Ketosis and ketonuria follow the failure to utilize sufficient carbohydrate and the consequent increased formation of ketone bodies from fat. The discovery of ketonuria in a

diabetic patient should always be taken as an emergency sign indicating the need for further study of the patient and prompt treatment. Although tests for acetone and diacetic acid may be strongly positive in the urine of some patients who have not as yet developed severe acidosis, ketosis is eventually accompanied by dehydration and loss of base. Numerous methods for ascertaining the degree of acidosis have been employed, such as determinations of the total acetone bodies in the blood, of the hydrogen ion concentration of the blood and of the excretion of ammonia in the urine. The degree of acidosis may also be determined accurately by measurements of the carbon dioxide content of the blood. If the carbon dioxide content of the blood has fallen from the normal of 26 millimols per liter (60 volumes per cent) to the neighborhood of 13 millimols (30 volumes per cent), a moderate degree of acidosis is present. When it has fallen below 9 millimols, experience indicates that, if unconsciousness has not already developed, its onset is a matter of hours and that the terminal stage of shock and anuria is impending.

In a recent article by Almy, Swift and Tolstoi\* the value of determinations of the blood-sugar and of the blood-carbon dioxide levels in the treatment of diabetic coma is minimized. In their series, however, since only 19 out of 99 patients had the typical Kussmaul breathing of acidosis, it is evident that the series included a large number of extremely mild cases of ketosis, although chemical data are not given. Indeed, only 1 patient was unconscious, and several of 7 who died had complicated cases. A more general teaching is that diabetic acidosis and coma are emergency states in which a careful study of the patient and chemical determinations of the sugar level and for evidence of acidosis in blood and urine are essential to the best type of treatment. A diagnostic pitfall to be avoided lies in the fact that, although ketonuria at first may be excessive, in the more advanced stages with renal failure, ketone bodies are no longer excreted in the urine. More emphasis should be laid on early diagnosis of impending diabetic coma, since treatment with insulin at that time averts the later and more critical stages. As pointed out by Dr Haigh in a letter published

\*Almy, T. P., Swift, K., and Tolstoi, E. Treatment of diabetic acidosis and diabetic coma. *J. A. M. A.* 129:863-868, 1945.

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## PEPTIC ULCER AMONG SOLDIERS IN THE MEDITERRANEAN THEATER OF OPERATIONS

LIEUTENANT COLONEL JAMES A. HALSTED, M.C., A.U.S., AND  
TECHNICIAN (5TH GRADE) HENRY WEINBERG, MED. DEPT., A.U.S.

AT THE beginning of the war, it was thought that peptic ulcer would present a serious military medical problem. This has evidently been the case in Army hospitals and induction centers in the United States. Owing to rejections at induction and discharge from the service of patients in Army hospitals in the Zone of the Interior, the disease was not seen in the Mediterranean theater of operations with the frequency expected, particularly after the first year. At the Sixth General Hospital in North Africa, however, to which a considerable proportion of patients were sent for evacuation to the United States, an opportunity was presented between March, 1943, and January, 1944, to study an unusually large number of patients with peptic ulcer.

Several reports<sup>1-3</sup> have appeared regarding the incidence and clinical features of this disease as seen in Army hospitals in the United States and in overseas theaters. In the present report are presented data in 200 consecutive cases among enlisted men. In certain aspects, the disease in these cases appears to differ from that noted among recent inductees in Army hospitals in the United States.

We have been interested in two main aspects of the problem—the purely clinical aspects and the psychosomatic features. In connection with the latter, certain data have been obtained bearing on the question of whether the nervous tension of Army life is a factor in either the etiology or the course of the disease. In addition, observations have been made regarding the personality differences between patients with peptic ulcer and those with chronic psychogenic dyspepsia; these observations appear to be of practical value in differentiating the two disorders.

### STATISTICS

The large number of soldiers with chronic epigastric distress admitted to the Sixth General Hospital in a period of ten months may be arbitrarily divided into those with peptic ulcer and those with dyspepsia not caused by ulcer, after excluding the cases in which the distress was caused by cholecystitis or some other abdominal disorder. Two hundred and twenty-four patients with proved

ulcer were admitted to this hospital, 24 of them were officers and are not included in this study. The exact number of patients with non-ulcer dyspepsia is not known, because many men had been on various services and had been discharged with varying diagnoses, particularly when the primary disorder was surgical, temporarily submerging the importance of the epigastric distress. A minimum figure, however, may be obtained from the total number of gastrointestinal x-ray examinations that were performed, since before disposition most of the patients with chronic indigestion were examined by x-ray in this hospital even though previously examined elsewhere. With the ulcer cases subtracted from the total number receiving gastrointestinal x-ray examinations, it is estimated that there were between 500 and 600 cases of non-ulcer dyspepsia. Thus, the ratio of ulcer to non-ulcer cases is about 1:3—a higher one than has been noted in most Army hospitals in the United States. The chief reason is that this hospital, being at the tip of a funnel for evacuation to the Zone of the Interior, received a considerable proportion of all ulcer patients in the theater. This ratio does not, therefore, signify that the incidence of peptic ulcer among soldiers with chronic epigastric distress is higher in the Theater of Operations than in the Zone of the Interior.\*

\*Since this paper was written we have had the opportunity to study patients with chronic dyspepsia at the Sixth General Hospital in Italy between July 1, 1944, and November 1, 1944. This hospital received patients from the front a few days after evacuation. Between November 1, 1944, and May 1, 1945, 350 patients with chronic dyspepsia were studied at a gastrointestinal center in the Fifth Army area. One hundred and eighty-three of these patients were studied roentgenologically by Captain S. M. Wyman, M.C., A.U.S. Among these 113 consecutive patients were x-rayed and gastroscopied to study the problem of gastritis, as well as to test the accuracy of the history alone in the diagnosis of peptic ulcer. The patients who were not x-rayed were diagnosed on the basis of the history and clinical observation.

At the Sixth General Hospital, where all patients were x-rayed, peptic ulcer constituted 8 per cent of the cases of chronic dyspepsia, as compared with 3 per cent at the gastrointestinal center of the Fifth Army. It would be expected that a higher percentage would be found at general hospitals, because they receive patients already observed clinically in whom the suspicion of ulcer is therefore greater. The low incidence at the gastrointestinal center, where nearly all the patients were infantrymen who had engaged in heavy combat, is strong evidence that combat does not cause peptic ulcer.

The 8 per cent incidence of peptic ulcer among patients with chronic epigastric distress encountered in North Africa can be explained by the fact that this hospital, owing to its position, received more ulcer patients than did any other at the time. The experience of other general hospitals in the theater, however, is similar to ours in that far more ulcer patients were seen in North Africa than in Italy. It is probable that many more cases of the disease were not disclosed by the screening processes carried out in the Zone of the Interior earlier in the war.

## CORRESPONDENCE

## DIAGNOSIS OF DIABETIC COMA

*To the Editor* It is regrettable that, even though a specific remedy has been available for nearly a score of years, patients still die of diabetic coma. Since the subject is no longer clouded by theories, not only unsound but useless, such deaths are inexcusable.

Too few of my interns and residents have grasped the simplest concept of diabetic coma: it is a fatal sign of immediate danger from what is essentially a deficiency disease, an insufficiency of insulin not merely in the blood but in every cell in the body. Hence the primary factor in treatment is the degree of acidosis, whereas hyperglycemia and dehydration are but secondary, even incidental. Accordingly, instead of repeated blood-sugar examinations, tests for ketosis are obviously more reliable guides to the amount of insulin needed promptly and directly to restore the deficiency and thereby save the diabetic patient. Simple tests for urinary acetone and diacetic acid are usually preferable to determinations of the blood-sugar level.

G W HAIGH

242 Burncoat Street  
Worcester 6, Massachusetts

## NOTICES

## ANNOUNCEMENTS

Dr Joseph S Barr, having returned from service with the United States Navy, has resumed practice at 234 Marlborough Street, Boston.

Dr Weston T Buddington, having returned from military service, announces the opening of his office for the practice of urology at 12 Bay State Road, Boston.

Dr S Forrest Martin announces the opening of his office at 101 Bay State Road, Boston, for the practice of ophthalmology.

Dr Channing S Swan announces his return to the private practice of urology with offices at 20 Gloucester Street, Boston 15.

## GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, March 12, at 8 15 p m. Dr Nathan Rosenthal, of the Mt Sinai Hospital, New York City, will speak on the subject "Blood Cell Reactions to Drugs." The paper will be discussed by Drs William Dameshek, Maxwell Finland, and Benjamin Alexander.

NEW ENGLAND HOSPITAL  
FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, March 7, at 7 15 p m in the classroom of the Nurses' Residence. Dr Eliza A Melkon will speak on the subject "Allergic Manifestations after the Injection of Varicose Veins," which will be followed by a discussion by Dr Eda A Polcari. Dr Dorothy K Scheidell will be chairman.

## JOSEPH H PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9-10 a m

## MEDICAL CONFERENCE PROGRAM

Friday, March 1 — Treatment of Psychiatric Problems  
Case discussion Dr Mandel E Cohen  
Wednesday, March 6 — Carcinoma of the Uterus Dr Louis E Phaneuf  
Friday, March 8 — Streptomycin Dr Donald Anderson

Wednesday, March 13 — To be announced Dr Harold A. Abramson

Friday, March 15 — Clinicopathological Conference Dr Chester S Keefer and H F MacMahon

Wednesday, March 20 — Diagnostic Errors in the Pratt Hospital Dr C B Popplestone

Friday, March 22 — First Stages of Human Conception Dr John Rock

Wednesday, March 27 — Roentgenological Changes in Sprue and Other Nutritional Disturbances Dr Alice Ettinger

Friday, March 29 — Some Aspects of Military Orthopedics Applicable to Civilian Practice Dr Joseph S Barr

On Tuesday and Thursday mornings, Dr S J Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr William Dameshek. Medical rounds are conducted by some of our staff members from 12 00 to 1 00 in the Lecture Hall.

All exercises are open to the medical profession.

AMERICAN ASSOCIATION FOR THE  
STUDY OF GOITER

The first postwar annual meeting of the American Association for the Study of Goiter will be held at the Drake Hotel, Chicago, on June 20, 21 and 22 — dates that are convenient for the majority of those planning to attend the meeting of the American Medical Association in San Francisco during the first week of July. Those who intend to be present at the Chicago meeting are advised to make their hotel reservations as early as possible.

## SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING  
THURSDAY, MARCH 7

## FRIDAY, MARCH 8

\*10 00 a m - 12 00 p m Medical Staff Rounds Peter Bent Brigham Hospital  
12 00 m - 1 00 p m Clinicopathological Conference (Boston Floating Hospital) Joseph H Pratt Diagnostic Hospital

## MONDAY, MARCH 11

\*12 00 m - 1 00 p m Clinicopathological Conference Peter Bent Brigham Hospital

## TUESDAY, MARCH 12

\*12 15 - 1 15 p m Clinicoroentgenological Conference Peter Bent Brigham Hospital

## WEDNESDAY, MARCH 13

\*10 30 - 11 30 a m Medical Clinic Isolation Building Amphitheater Children's Hospital  
\*12 00 m Clinicopathological Conference (Children's Hospital) Amphitheater, Peter Bent Brigham Hospital  
\*12 00 m - 1 00 p m Clinicopathological Conference Cambridge Hospital  
\*2 30 - 4 00 p m Combined Clinic by the Medical Surgical and Orthopedic Services Amphitheater Children's Hospital  
\*7 15 p m Graduate Seminar in Pediatrics Children's Medical Service, Amphitheater 3A Massachusetts General Hospital

\*Open to the medical profession

JANUARY 7-APRIL 22, 1946 Metropolitan State Hospital Eleventh Postgraduate Seminar in Neurology and Psychiatry Page 314 issue of September 6

FEBRUARY 4-MARCH 29 Health Education Institute Page 746 issue of December 13

MARCH 1-MARCH 29 Joseph H Pratt Diagnostic Hospital Medical Conference Program Notice above

MARCH 7 New England Hospital for Women and Children Notice above

MARCH 11 Massachusetts Hospital Association Page 240 issue of February 14

MARCH 12 Greater Boston Medical Society Notice above

MARCH 14 Baristas at the Shoulder Joint Diagnosis and treatment Drs Francis C Hall and Robert B Osgood Pentucket Association of Physicians 8 30 p m Haverhill

MARCH 15-SEPTEMBER 15 Boston University Course for Discharged Medical Officers Page 240 issue of February 14

APRIL 1-JUNE 1 Intensive Course in Ophthalmology Page 240 issue of February 14

APRIL 4 Hermann M Biggs Memorial Lecture Page 206 issue of February 7

MAY 13-17 American College of Physicians Page 798 issue of December 20

JUNE 20-22 American Association for the Study of Goiter Notice above

DISTRICT MEDICAL SOCIETY  
WORCESTER

MARCH 13 Worcester Memorial Hospital

APRIL 10 Habnemann Hospital

MAY 8 Annual meeting

dyspepsia, the mental reactions of the vast majority of the patients with peptic ulcer were strikingly different from those of the non-ulcer patients. Most of the latter were anxious to describe their symptoms in detail, whereas the ulcer patients were noncommittal and unconcerned with themselves, other than for the single definite symptom—pain. In other words, the symptomatology of the patient with psychogenic dyspepsia was a direct expression of his anxiety and insecurity, whereas that of the patient with ulcer had no direct connection with anxiety. In making ward rounds, it was noted that the ulcer patients rarely complained or volunteered information regarding the degree of pain unless direct questions were put. From these observations alone it has been possible to predict with a considerable degree of accuracy what x-ray examination will reveal in patients with chronic epigastric distress, regardless of whether the symptoms were typical or atypical of ulcer. In most cases it could be predicted that the x-ray film would be negative in those patients who were anxious and unduly concerned with their stomach symptoms. Only rarely was an ulcer diagnosed by x-ray when the clinical impression had been that the patient did not have an ulcer. Much oftener a clinical impression of ulcer was not substantiated by x-ray. This lack of anxiety in the ulcer patients is in contrast to the findings of Flood,<sup>9</sup> who reports that 25 of 47 ulcer patients at the Station Hospital, Fort Meade, who had been studied neuropsychiatrically presented signs of anxiety. Schildkrout<sup>10</sup> reports 23 per cent of 87 cases of duodenal ulcer studied at a staging area in the United States, as having a psychoneurosis.

The symptomatology of the patients in this series was considered typical of ulcer in 72 per cent of the cases, that is, there was a characteristic indefinable, dull pain in the epigastrium, coming on one or two hours after meals and often in the middle of the night, which was relieved by food. Vomiting was an infrequent symptom. The symptomatology of the non-ulcer patients, although often resembling that of the ulcer patients with atypical symptoms, was rarely typical of ulcer. In patients who had had an ulcer for but a short time, the symptoms as related by the patient were often atypical—much more frequently so than in those who had had the disease for a long time.

The family history was ascertained in 167 patients. In 74 (44 per cent) some member of the immediate family had had chronic digestive difficulties. A similarly high incidence of familial predisposition to chronic indigestion has been noted in all studies of peptic ulcer. Whether this tendency is the result of a constitutional predisposition or carries a psychologic implication is uncertain.

The physical examination was negative in the vast majority of cases except for moderate epi-

gastric tenderness, which was present in most cases. The x-ray examinations demonstrated a crater in 48 per cent of the cases so examined.

We were interested in the therapeutic response because of the lack of ideal facilities for treatment. Careful data could not be collected because the hospital stays before evacuation by transport to the Zone of the Interior were too short, being as a rule not more than two weeks. In the majority of cases, however, the degree of pain and discomfort was promptly lessened, usually within two or three days, and from then on the patients were quite comfortable.

The treatment instituted was the same in nearly all cases. Six-meal bland diets were provided, tincture of belladonna and alkaline powders being given as needed. The diet was limited in variety and not particularly palatable, owing to problems of supply. Feedings between meals consisted of powdered or evaporated milk, with or without crackers. Nearly all the patients were ambulatory. On admission, only 2 patients required complete bed rest with hourly feedings of milk. A few more were given for a few days two-hourly feedings of milk, with cereal, custard and crackers for the main meals. Tobacco was not prohibited. By and large, the symptoms of the entire series of patients were mild, responding promptly to the relatively crude dietary measures available. This finding is in contrast to Flood's<sup>9</sup> observation that the patients studied at the Station Hospital, Fort Meade, responded poorly, both symptomatically and roentgenologically. Our patients responded to treatment much as one would expect in such cases in civilian practice. Flood considered that the factor of anxiety, occasioned or intensified by the rigidity of Army life and by uncertainty for the future, was responsible for the poor response to treatment in his series, which was chiefly composed of recent inductees. The 11 patients who had had long Army service, on the other hand, responded well to treatment except for 2 who were highly neurotic. The patients in our series had had full military training and had come to a theater of operations. As soon as the diagnosis had been established they were told that they were to be sent home, so that the anxiety factor was largely removed. Thus, the good response to treatment when the anxiety factor was minimal, in contrast to the poor response in a different series in which this factor was relatively strong, is confirmatory of the prevailing belief that psychogenic factors are of importance in peptic ulcer.

In contrast to the almost universally good symptomatic response of patients with peptic ulcer to dietary treatment and hospital care, patients with psychogenic dyspepsia rarely improved symptomatically as a result of these measures. This observation provides a valuable clinical test in differential diagnosis.

Because the functions of Army hospitals often differ and because the nature of the work of this hospital has changed from time to time, a comparison of statistics with those of other reports in the literature would not be contributory. It appears, however, that the figures from this hospital are roughly the same as those in other American and British reports<sup>4</sup>, as regards the incidence of gastro-duodenal disorders as a whole in respect to total medical admissions. The British consistently report a far higher ratio of peptic ulcer to non-ulcer dyspepsia than is found in American reports. The reasons for this discrepancy are not clear. It is certainly true that chronic dyspepsia and peptic ulcer together form an important military medical problem, although in the Mediterranean Theater the former was much the more important of the two.

A study of chronic non-ulcer dyspepsia cases in this hospital has been made and reported elsewhere<sup>6</sup>. That study was primarily an investigation of psychiatric factors in etiology. It was found that in more than three fourths of the cases the cause was psychogenic, that is, definite psychogenic factors were present with no other organic explanation. In the remainder of the cases positive evidence of significant neurotic factors was lacking, although there was likewise no demonstrable organic cause. In cases with definite psychogenic factors the diagnostic term "psychogenic dyspepsia" was employed. Among a few of the remainder a later follow-up with subsequent study revealed that many of these cases were likewise psychogenic in origin. It was found that patients with psychogenic dyspepsia who had been long in hospitals could rarely be salvaged for further military service. It was further noted that the personality structure of a large majority of patients with chronic psychogenic dyspepsia was basically different from that of a large majority of patients with peptic ulcer.

#### METHOD OF STUDY

The large number of patients with peptic ulcer observed in a relatively short time forbade prolonged study, but data concerning the onset of the disease, with the possible influence on its course of various factors in the Army career, were accurately ascertained. Thus, in every patient the following data were noted: age, rank and branch of service, length of service, the duration of symptoms from the patient's earliest recollection of persistent indigestion (this was considered to be the onset of the disease), whether symptoms were aggravated on entrance into the Army, provided the disease had begun prior to induction, the date of departure for overseas service, whether symptoms had become aggravated coincident with overseas service (a period of time from two weeks before embarkation to four weeks after debarkation was arbitrarily chosen as the time of greatest nervous tension that might influence the symptomatology), and

whether the patient had been in combat and, if so, whether he had been wounded. In addition to these data, it was noted whether the symptoms were typical or atypical of peptic ulcer and whether there was a family history of ulcer or chronic indigestion.

In 100 patients, a detailed history was taken, attention being paid to factors of emotional or neurotic significance. Thus, all phases of the past history were investigated, including the family history and the educational, occupational, social, marital and military phases of the patient's life. These patients were interviewed by one of us (H W), a psychologist on the Neuropsychiatric Service, to make a further personality study. Both of us then discussed the findings that each had made independently. An average of two hours' time was spent on the history and personality study of each patient. The purpose of this investigation was to evaluate the nervous and emotional factors that might be present in the personality pattern of the ulcer patient and to compare them with the findings made in 100 patients with chronic non-ulcer dyspepsia who were being studied at the same time in a similar manner.

The laboratory studies included stool examinations and blood-cell counts when indicated, and occasionally gastric analysis. The latter test was considered to be of relatively little value in the diagnosis, treatment or prognosis of peptic ulcer, except in cases with gastric lesions, in which x-ray examination alone does not always enable one to differentiate ulcer and carcinoma and in which the presence or absence of free hydrochloric acid is significant. This viewpoint is in agreement with that of Schindler<sup>6</sup> and Alvarez<sup>7</sup> (but not with that of Chamberlin<sup>8</sup>), each of whom has recently discussed the value of the procedure in Army gastroenterology. The test was performed only in patients with gastric ulcer, in the few patients who did not readily respond to treatment and in 3 patients with duodenal ulcer in whom anacidity had been reported from other hospitals. Free acid was found in the last group when histamine was employed as a stimulant.

As previously noted, it was our policy to make x-ray studies on all patients with chronic epigastric distress. A few patients who had come from other general hospitals and whose records and clinical findings indicated entirely satisfactory evidence of an active ulcer were not again x-rayed. No patients were included in the series who did not have a constant deformity of the duodenum or a crater. In many questionable cases the examination was repeated two or three times. Spot films with compression technic were taken in nearly all cases.

#### CLINICAL ASPECTS

##### *Clinical Findings*

In the taking of histories of patients with chronic

these patients were promptly hospitalized and sent home, but the majority paid no attention to the symptoms, remaining on duty until the symptoms had become extremely severe and often engaging in combat without reporting to sick call. In 87 cases (44 per cent), the disease began after entry into the Army. In 50 of these (25 per cent), it began after the patient had started for or arrived in the Theater of Operations. Twenty-four of the 37 patients whose ulcers had begun after entry into the Army but before coming overseas reported that their symptoms became much worse shortly after starting for overseas service. Thus, of 150 patients who had peptic ulcer before going overseas, in 103 (69 per cent) an aggravation of symptoms or recurrence of the ulcer could be directly correlated with nervous tension.

The 150 patients who had peptic ulcer prior to embarkation should theoretically have been excluded from overseas service. The reason why they were not may lie in the fact that most ulcer patients observed in overseas areas are restless and aggressive, and frequently conceal or minimize symptoms in order to be accepted in the Army or to be sent overseas. Berk and Frediam<sup>16</sup> state that their patients, who had not been overseas, did not conform to this type, that many were of low intelligence and that many made use of their ulcers to secure discharge from the Army. Thus, it may be that the ulcer patient who gets overseas is a different type of person in respect to aggressiveness.

Almost every patient's explanation of the recurrence or aggravation of his symptoms in the Theater of Operations was the difficulty of digesting the field rations on which he was obliged to subsist. That the accuracy of this is debatable is shown by the fact that the symptoms of many of these patients began or became aggravated at the port of embarkation or on the transport, and that when this occurred in the Theater of Operations it was not until they were subjected to the strain of air raids for the first time or started for the front, having been in the combat area and having eaten field rations for some time. This suggests that the main reason for the recurrence or aggravation of symptoms of peptic ulcer in these patients is not the type of food eaten but the nervous tension involved in overseas service.

#### DISPOSITION OF PATIENTS

The patient with peptic ulcer as seen in the Theater of Operations is a highly successful soldier who as a rule has had his symptoms for a considerable period of time without complaining to a medical officer. The disease is clinically mild, and there have been relatively few complications. These patients have been of much greater value to the Army than the dyspeptic patients without organic disease. Yet it has been the practice promptly to send home practically every ulcer patient, where-

as patients with non-ulcer dyspepsia are usually returned to duty or limited service, even though their disorder is generally more disabling and less amenable to treatment than peptic ulcer.

Patients with peptic ulcer in a theater of operations should in the large majority of cases be sent to the Zone of the Interior, because the chances of recurrence are extremely great and management of the disease outside a hospital is almost impossible. In this series, however, there were 6 patients in base organizations whose symptoms disappeared promptly and who were anxious to be returned to duty. After four to six weeks of hospitalization this was done. In view of the mildness of the disease as seen in this theater, the high military quality of most of the patients and the fact that in the United States nervous tension is lower and dietary conditions are better, it seems probable that many of the ulcer patients sent to the Zone of the Interior could be successfully utilized in a noncombat status within the United States after a few weeks of hospitalization.

#### PSYCHOSOMATIC FEATURES

In the foregoing sections certain statements regarding psychosomatic features have been made, inasmuch as they had an important bearing on the clinical aspects of the disease. These may be summarized as follows:

The extremely low incidence (3.4 per cent) of peptic ulcer among combat infantrymen hospitalized because of chronic dyspepsia is strong evidence that combat is not a factor in the cause of this disease. The reaction of patients with ulcer differed markedly from those with non-ulcer dyspepsia in that the latter were emotionally concerned with their stomach symptoms. Patients with a neurotic reaction rarely proved to have ulcer, even though the symptomatology resembled that of ulcer. Patients with peptic ulcer responded rapidly and satisfactorily to a crude dietary regimen. This differed from the response to treatment of a group in a station hospital in the Zone of the Interior, which may be interpreted as having been due to the patients' security in the knowledge that they were to be sent home. Lastly, there was a close correlation between aggravation of symptoms in a presumably active ulcer or recurrence of activity in a previously quiescent one, and the nervous tension associated with going overseas. Such a correlation was present in 103 of 150 patients.

It is believed by many workers that peptic ulcer is a psychosomatic disease in the sense that emotional disturbance with chronic nervous tension is an important factor, if not the primary one, in the etiology of the disease. No conclusive evidence can be drawn from the statistical data of this report in support of such a contention. Nearly 45 per cent of these patients developed ulcer after entry into the Army, and 25 per cent did so after coming



## Type of Ulcer

There were 188 cases of duodenal ulcer (94 per cent) and 12 cases of gastric ulcer (6 per cent), the latter incidence being essentially the same as that reported by Flood<sup>9</sup> and Annis<sup>11</sup> from two station hospitals in the United States. In the 12 cases of gastric ulcer (Table 1), the lesion was on the lesser

TABLE 1 Data on Cases of Gastric Ulcer (12 Cases)

CASE No.	AGE	RACE	LOCATION	DURATION	REMARKS
1	45	White	Lesser curvature	5 mo	
2	26	White	Prepyloric area	1 mo	Perforation
3	53	Negro	Prepyloric area	2 yr	Gastric resection possible malignancy
4	37	Negro	Lesser curvature	2 mo	
5	45	White	Lesser curvature	3 mo	
6	54	Negro	Prepyloric area	4 mo	
7	37	White	Antrum	8 mo	
8	24	Negro	Lesser curvature	1½ mo	
9	37	White	Lesser curvature	11 mo	
10	26	White	Prepyloric area	7 mo	Perforation
11	30	White	Prepyloric area	3 mo	
12	24	Negro	Lesser curvature	5 days	Subacute perforation (no operation)

curvature in 6 cases, in the prepyloric area in 5 — in 3 of which it was confirmed by operation — and in the antrum in 1 case. In 9 of the gastric ulcer cases the ulcer occurred after arrival overseas. These cases represented 18 per cent of the 50 cases in the entire series in which peptic ulcer developed after arrival overseas, as compared with 2 per cent of those in which disease had existed before going overseas.

## Racial Distribution

There were 16 Negroes with peptic ulcer, or 8 per cent of the series. This is probably a normal incidence, taking into account the small proportion of Negro troops in this theater. It does not substantiate statements that have been made to the effect that Negroes are less prone than Whites to develop this disease. In 10 of the 16 Negroes (62 per cent), the onset occurred after arrival overseas. There were 5 cases of gastric ulcer among Negroes, or 42 per cent of the number of these ulcers in the series, a surprising and inexplicable percentage, considering that only 8 per cent of the 200 patients in the series were Negroes.

## Age, Rank and Branch of Service

The ages of the patients were neither greater nor less than the average for the Army as a whole. One hundred and seventeen patients (59 per cent) had received at least one promotion. Seventy-two per cent of the patients belonged to combat branches of the Army. Fifty-four patients had engaged in a slight to moderate amount of combat, and 9 had been wounded, none severely.

## Complications

As noted previously, all the patients in this series had been sent to this hospital from other hospitals,

where they had been treated initially. Because of this, there was only 1 case of major hemorrhage and 1 of subacute perforation. In the former case, the bleeding had begun on a transport from which the patient was transferred directly to this hospital, still bleeding moderately. A history of massive hemorrhage since arrival in this theater was obtained in 7 cases and one of perforation in 9 cases, the latter having been the first sign of the disease in 3 cases. Three of the cases of perforation were those of patients with gastric ulcer, and in 2 of these the perforation was in the prepyloric region, as verified at operation. The third patient, a Negro with an ulcer in the lesser curvature, was thought to have had a subacute perforation, since he had had severe pain at onset, with low fever and leukocytosis persisting for three weeks. He was not operated on.

It has been noted that the incidence of perforation in the civilian population of London during the two months of heaviest air raids in September and October, 1940, was three times as great as the normal average.<sup>12</sup> It has been thought that massive hemorrhage is especially frequent during periods of extreme nervous strain. The incidence of perforation and that of hemorrhage in this series — 4.5 and 3.5 per cent respectively — are not high, being essentially the same as those reported by Thomas<sup>13</sup> among 75 cases from Fort Meade. If psychogenic factors are important as precipitating causes for these complications, as suggested by Stewart and Winsor,<sup>12</sup> the low incidence in this series may be due to the fact that the military population was composed of trained, disciplined soldiers.

Pyloric obstruction occurred in 3 patients, 2 of whom required gastric resection before they could be sent home.

## Onset of Disease in Relation to Army Service

Reports in the literature on soldiers with ulcer studied in the United States agree that in 90 per cent the ulcers occurred prior to entry into the Army.<sup>9, 14</sup> This is in accordance with British figures.<sup>15</sup> According to Chamberlin,<sup>14</sup> these patients reach the hospital on an average of five months after induction. Ninety-three per cent of Flood's patients, who were recent inductees, had had symptoms prior to induction. Essentially all this group were discharged from the Army. The results of our inquiry into the onset of the disease in relation to time of entry into the Army are quite different.

In 113 patients (57 per cent) there was a history of unexplained indigestion or symptoms resembling those of peptic ulcer prior to entry into the Army. In 33 of these patients, a recurrence or aggravation of symptoms occurred within four weeks after entry into the Army, but not many of them sought medical attention. In 79 cases, recurrence or aggravation occurred shortly after arrival overseas. A few of

have been so striking as to leave no doubt that they actually exist. The main personality features that have been described were surprisingly uniform and definite. In the regimented life of the Army, when all men live exactly alike, exposed to the same difficulties and the same needs for adjustment, and where the opportunities for compromise existing in civilian life are lacking, the differences are doubtless far more obvious than they would be in civilian practice. Additional studies of patients of the latter sort, both men and women, are needed to confirm or disprove the conclusion drawn from this study of men living under regimented conditions, to the effect that those who develop peptic ulcers have a personality pattern fundamentally different from that of those who develop psychogenic dyspepsia.

If one accepts the hypothesis that psychogenic factors are important in the etiology of peptic ulcer, it is illogical to assume that psychogenic dyspepsia, in which the personality type differs markedly from that in peptic ulcer, should develop into the latter. Schildkrout<sup>10</sup> and Urquhart<sup>19</sup> have commented on the low incidence of functional dyspepsias that later develop ulcer, the latter finding it to be less than 3 per cent. If such did occur, one would expect combat infantrymen to develop the disease in large numbers, inasmuch as psychogenic dyspepsia is extremely frequent among them,<sup>17</sup> yet it is extremely rare.

On the other hand, that peptic ulcer is a psychosomatic disease is not yet proved. The above data, both statistical and psychiatric, are consistent with such a theory, yet add no conclusive supporting evidence. The discrepancy between our findings and those of Flood,<sup>9</sup> Berk and Frediani<sup>16</sup> and Schildkrout<sup>10</sup> on soldiers with ulcer in the United States as regards personality factors and response to treatment has several possible explanations, among which are the following. Standards of psychiatric evaluation, always largely subjective, may have differed. Environmental factors are known to affect the form of any psychologic reaction. For example, severely wounded soldiers react quite differently to pain from civilians with comparable injuries. Finally, it may be that the man with pre-existing ulcer who manages to get overseas is actually a more aggressive, effective soldier than those who remain in the United States.

It is hoped that the observations reported herein may be of use in integrating the many factors involved in the psychosomatic aspects of peptic ulcer. Much further work will be required before a psychogenic factor can be assigned a specific major role in the etiology of this disease.

#### SUMMARY AND CONCLUSIONS

A clinical study has been made of 200 consecutive cases of peptic ulcer seen in a general hospital in the Mediterranean Theater of Operations. The

disease was mild, and the response to treatment was prompt and satisfactory, being similar to or more favorable than that observed in civilian practice. The incidence of major complications was no higher than that noted among soldiers in the United States.

A study of psychosomatic features revealed that distinct episodes of nervous stress could be correlated with an aggravation of symptoms or recurrence of previously existing ulcer in 69 per cent of 150 patients whose disease had begun before coming overseas. Only 3.4 per cent of 183 combat infantrymen with chronic epigastric distress had peptic ulcer. The disease was more frequent among base troops than among combat troops.

Forty-four per cent of the patients developed the disease after entry into the Army, and 25 per cent developed it after beginning overseas duty. Reasons are given for believing that these figures are not significant as indications that the nervous tension of Army life is a direct factor in etiology of new ulcers.

The results of a psychiatric study of 100 patients were consistent with those of previously reported work on the personality pattern of patients with peptic ulcer. This pattern was markedly different from that of the large majority of patients with psychogenic dyspepsia, and is valuable as a differential point between the two disorders.

Reasons are given for believing that psychogenic dyspepsia does not evolve into peptic ulcer.

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overseas This is in contrast to reports from Army hospitals in the United States, where 90 to 95 per cent of patients with ulcer had had the disease prior to entry into the Army, and suggests that the nervous tension of Army life is at least a contributory cause of the disease This difference may, however, be explained otherwise The incidence of the disease is normally highest in men of military age With the screening out of a large number of men with old ulcers in the United States before their units were sent overseas, the percentage of new ulcers that would normally be expected to develop in this age group should be higher in men who have been sent overseas because they have been longer in the Army

Subsequent information obtained at the end of the war in Europe revealed that the incidence of peptic ulcer in the entire Mediterranean Theater of Operations was low, and probably lower than the expected incidence for men of military age

New peptic ulcers were rare among infantrymen exposed in Italy to part of the most intense and difficult combat of the war This indicates that fear, with the associated nervous tension, is not a factor in the etiology New ulcers were seen more frequently among base troops than among combat troops, and this suggests that the frustration of regimentation with frequent periods of inactivity may be more damaging than actual danger, in which there are opportunities for release of energy through aggressive action

It was to study the psychiatric features of patients with peptic ulcer that the personality study of 100 patients, described above, was made From a psychiatric viewpoint, the study was a superficial one, since many hours with each patient would have been required to make an accurate and deep survey Nevertheless, as a result of both the interviews and the observations of the patient's reactions made on daily ward rounds, it was possible to determine whether the patient was neurotic, to obtain data regarding his past environment and to get a clear picture, at least on a superficial level, of his characteristic personality pattern This could be contrasted with that of the patient with psychogenic dyspepsia The marked differences noted have proved to be of practical value in differential diagnosis Many patients with psychogenic dyspepsia have no apparent anxiety, their only complaint being epigastric distress In the Army, hospitalization of such patients is harmful, inasmuch as symptoms grow more fixed the longer they are studied and treated from a medical rather than a psychiatric standpoint Early diagnosis and disposition from medical channels at forward hospitals, in many of which x-ray facilities are not available, has been shown to be of marked military value, as well as of definite therapeutic value, in such patients<sup>17</sup>

Data regarding the background of the patients

with peptic ulcer revealed two important features suggestive of emotional insecurity Thirty-nine per cent of the patients had had an unfavorable childhood environment, such as separated or incompatible parents or severe economic distress resulting in neglect Nineteen of 49 patients who had married were divorced or separated Other factors that could be analyzed statistically were perhaps no more prominent than those to be found in any random group of men Thus, 13 per cent of the patients had had enuresis in childhood, 20 per cent gave a history of anxiety phobias, such as fear of high places, of the sight of blood or of accidents, 20 per cent drank somewhat excessively on occasion, and 19 per cent had mild or moderate psychosexual conflicts

Despite the presence of neurotic factors in a considerable proportion of the patients, only 5 per cent demonstrated a clinical neurosis In other words, the large majority were not disabled by whatever neurotic traits were present The patients with neuroses were abnormally concerned with their gastric symptoms, which seemed to have emotional value for them, and also showed evidence of anxiety More extensive investigation would perhaps have disclosed in a larger number of patients significant neurotic features of an aggressive type with overcompensation This has been demonstrated by Mittelman, Wolff and Scharf<sup>18</sup>

It has often been stated that the patient with peptic ulcer tends to be an unrelaxed, hard-driving, overaggressive person We have noted this to be true as a general trend among our patients In spite of a surface appearance of self-sufficiency, the characteristic ulcer patient, as we have observed him, is not relaxed and is not free of anxiety, as has been noted by other writers He is not normal in his behavior and feelings, although his abnormal temperament leads to material success This generalization is based on the fact that most of these patients when asked if they often felt nervous complained of being restless and unable to relax The behavior on the ward of the large majority of patients was one of restlessness and impatience, thus confirming this statement The ulcer patient, however, seems to solve his underlying insecurity differently from the patient with psychogenic dyspepsia In contrast to the latter, he has developed an abnormal drive combined with restlessness and impatience, by which he controls his anxiety The dyspeptic patient magnifies his every illness and is overcome by it, whereas the ulcer patient shows an apparent indifference to the whole affair Our ulcer patients conformed to the description given by Mittelman, Wolff and Scharf,<sup>18</sup> whose patients showed assertive independence and self-sufficiency, covering underlying anxiety and insecurity and accompanied by feelings of resentment and hostility

These differences between the two groups, although gained from a superficial personality study,

fects in this initial surgery. We have been impressed by the speed with which these wounds first come to débridement and by the excellent work done by the evacuation hospitals. Sometimes, of course, through force of circumstances, delay is unavoidable and débridement is incompletely done. This is always apparent in the condition of the wound and necessitates the placing of preliminary wet dressings before closure can be attempted. Bits of foreign material have sometimes been found in such wounds when it was obvious that the pressure of casualties had allowed less careful treatment. The desirability of adequate débridement needs no emphasis to the tireless workers who have done such perfect work in the advance units. Testimony of the effectiveness of their work is furnished by the fact that a large percentage of wounds reached us in such perfect condition as to permit immediate closure.

#### *Intermediate Dressings*

Most patients consider that a surgical dressing is evidence of careful medical attention. That wounds should be débrided and dressed seems reasonable to the layman. A white gauze bandage quickly becomes soiled, is frequently loosened and is usually blood stained. To remove this unsightly dressing and apply a clean, firm, fresh one pleases most patients and too many physicians. That every change of dressing, even under the most favorable conditions and with the best aseptic technic, means introduction of infection is a fact not sufficiently recognized, and when the conditions are not so ideal and the technic not so scrupulous, the danger is considerably increased. One needs only to observe the contrast in the clinical appearance of wounds coming to a general hospital to appreciate this fact. The ideal wound for closure is the one which has its débridement dressing removed in the operating room just before suture. Most wounds associated with fractures and therefore encased in plaster casts, which effectively discourage intermediate dressings, are cleaner than simple flesh injuries, even though they are generally much more extensive. Perhaps all débrided wounds should be dressed with a light plaster, which would afford greater protection to the damaged tissues and be more resistant to soiling and disarrangement, and thus less likely to invite a change of dressing. Certainly intermediate dressings should be discouraged unless there is a definite indication for them, such as fresh bleeding or systemic evidence of infection.

#### *Chemotherapy*

All patients received through American installations had already received chemotherapy in some form. Penicillin has been given routinely for forty-eight hours after closure, but not after that time except for specific indications. The excellent condi-

tion in which the ideally treated wound is found is considered in some measure due to previous chemotherapy. Certainly when one sees extensive abdominal wounds and patients with multiple compound fractures, the wonder frequently is that they have survived long enough to reach a general hospital. There can be little doubt that many of these patients owe their lives to early chemotherapy. Once they have reached this hospital, an adequate defense mechanism has been established, and only enough penicillin is needed to tide them over whatever breakdown of the walling-off process is incident to the secondary closure.

#### *Method of Closure*

As indicated above, we prefer to book candidates for secondary closure without prior inspection and to have the dressing initially removed on the operating table. On removal of the vaseline gauze with which the wound should be loosely packed, the tissue should be beefy red, with no foreign material and no suppuration or slough. The skin borders should be pliable and elastic, with no surrounding induration or inflammatory reaction. Usually the general appearance of the wound invites closure. Some wounds have a mild grayish exudate with a slightly glistening sheen, which has not been found to be a danger signal. We do not apply antiseptics to the area or even wash out the wound itself. The wound is covered with a sterile sponge while the surrounding skin area is being prepared. In most cases preparation consists of painting the wound with two coats of Tincture of Merthiolate and one of alcohol. If the dressing has been disarranged and the area around the wound thus contaminated, it is cleaned with a sponge moistened with tincture of green soap or ether before applying the antiseptic solutions. It is thought that too vigorous scrubbing of the area may wash bacteria into the wound, so that the skin is washed at this time only when such a step is visibly indicated. The wound itself is not prepared in any way. The presence of a little vaseline does not interfere with the healing of closures or with grafting procedures.

It takes some experience to judge whether a wound is of suitable size and shape for direct closure. With more experience, it will probably be possible to apply this procedure to seemingly hopeless cases. It has been found that even considerable tension is tolerated if other conditions are favorable. Looseness of the skin is a distinct advantage. Wounds of the back, chest, abdomen and thighs are more easily closed than are much smaller ones on the forearm or lower leg. Special caution has been observed in dealing with wounds of the buttocks, and in many cases it has been considered best to strap them with fenestrated adhesive strips. This method in fact produces almost as good a closure as does suturing, and it is preferable when there is any possibility of sepsis. It has the advantage of

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## THE RESULTS OF SECONDARY CLOSURE

LIEUTENANT COLONEL PHILIP S. FOISIE, M.C., A.U.S.\*

IT HAS been observed that the victory in World War II is likely to be credited to penicillin and secondary closures. The humor of this remark detracts in no way from the importance attached to these surgical aids by those who have witnessed their proper application.

During the last nine months we have done secondary closures on 1450 patients, these closures constituting 43 per cent of all operative procedures. Since many of these patients had multiple wounds, as many as thirty wounds having been closed in a single case, the total number of wounds closed is well over two thousand. It would be meaningless to give over-all percentages of results regardless of the antecedent histories, since this would combine the favorable cases having a normal expectancy with those presenting little hope of success, and thus give a true picture of neither group. Because of the vicissitudes of the process of evacuation, patients have arrived with every conceivable type of wounds — early and late ones, those not touched since their débridement and those frequently dressed, wounds with accompanying trauma to blood vessels, nerves, tendons and bone, and wounds of all sizes and shapes and in all locations. As regards cases with extensive loss of tissue and exposure of important structures, the choice of the appropriate plastic procedure requires discussion in specialized articles, but the ordinary flesh wound needs primary consideration because the basic principles of its treatment apply in almost all war injuries.

Our introduction to battle casualties gave us a mixed group of cases many of which were too old for successful closure. These received wet dressings and many of them were finally closed, but we seldom obtained better results than an indurated scar having wide suture marks and causing difficulty in mobilizing the adjacent joints. It was obvious that once a wound became infected the end result would be impaired even though the wound were properly cleaned before closure. It was equally obvious that open wounds would become infected even with careful dressings. The logical answer seemed to be to close the wound at the first dressing after débridement. It has been our policy to do this whenever possible, and experience indicates that it gives the best results.

After the first convoys mentioned above had arrived, we received patients evacuated by air, many of whom had wounds that were only two or three days old. These cases were scheduled for

operation without even preliminary ward inspection. This policy caused a few "dry runs," but it was believed that the advantage gained in the large majority of cases warranted this inconvenience. There were occasional small wounds that did not require closure — cases with perforating small-arms wounds in which it was not desirable to seal up a long tract and with odd septic wounds. Cases with a favorable history, that is, one of adequate and prompt débridement and no intervening dressings, amounted to no more than 5 to 8 per cent of the total.

As the battle front got farther away, cases as old as three or four weeks again began to arrive. These had usually been dressed many times, and the incidence of infection was so high that it was no longer permissible to close them immediately, and it was necessary to revert to preliminary wet dressings, with a corresponding worsening of end results. The evacuation pendulum finally again swung in our favor, and recent convoys have brought in patients with wounds four, five and six days old. Once more the operating rooms were kept going at full speed so that all these wounds could be closed at the first dressing. The results were satisfactory.

This varying experience has shown that the results of secondary closures can be quite accurately predicted on the basis of the conditions under which the operation is performed. With a prompt and adequate débridement and no intervening dressings, wounds that are closed by the end of the first week have healed without complications in 95 per cent of cases. In less than 2 per cent of such cases frank sepsis has been encountered. Only 3 per cent have developed hematomas that had to be evacuated. Moreover, these wounds heal with a minimum of induration and inflammatory reaction. After ten days, as the number of intervening dressings and the time interval between them increase, there is a corresponding decrease in the percentage of wounds that can be closed at the first dressing, reaching zero in about three weeks. In the cases of this group and those that are closed after being cleaned, a percentage of satisfactory results of 60 per cent is the highest that can be expected. Here one encounters much more drainage, breaking down of all or a portion of the wound and considerable inflammatory reaction, cutting in of sutures and finally greater scar contracture.

### Débridement

The value of prompt and complete débridement is easily seen at the time of attempted closure. The pressure of action at the front is quickly re-

\*Assistant to visiting surgeon, Boston City Hospital; instructor in surgery, Tufts College Medical School (on leave of absence).

study medicine. They were eventually assigned to civilian hospitals or trained as specialists. It was evident that the various professors did not desire women as their assistants or as students for prolonged training leading to eventual certification in a specialty.

Thus, the main difference in the selection of students, as compared with the prewar method, was that the majority were admitted by appointment from an outside authority. There was no apparent screening by an entrance board, and many students who had a natural aptitude and desire for the study of medicine never had the opportunity to enter medical school.

### *Undergraduate Training*

Without question, the war drastically interfered with the training of medical students. In the first place, the total length of study — premedical and medical — was decreased from six years, or twelve semesters, to five years, or ten semesters. Finally, early in 1945 it was further reduced to four and a half years, or nine semesters. Since the majority of the students were under control of the Army, they had many interruptions associated with military training and Nazi Party functions. At least one semester of the premedical years was spent by the student as a medical corpsman at the front. During the three medical years he had to spend approximately two semesters working in an Army hospital at the front. Probably the students with considerable previous military service were excused from some of these assignments. There seemed to be no systematic arrangement for the assignment of these students to Army service for any given period of time. Apparently, groups were sent throughout the year for periods ranging from a few weeks to three months. Ordinarily, in the years of clinical study they would have worked for a period of three months in each of the various clinics, such as those of surgery, medicine and otolaryngology. As a result of this Army service, many must have missed the opportunity for bedside teaching and clinical work in hospitals other than that afforded at the front. Certainly, no faculty under the circumstances could have juggled a curriculum to cover the needs of such a fluctuating student body. The total time actually spent in the university, including the premedical and medical terms, was in reality limited in the majority of cases to about three and a half years.

The effect of the above-mentioned factors alone was sufficient to produce a drastic lowering in the quality of medical graduates. There were, however, other serious influences, which were brought out by all the professors. They emphasized the effects of the general hardships of a prolonged war and the attitude naturally associated with war as distracting even the better students from serious study and application. Education had been further interfered with, especially during the previous

eighteen months, by air-raid alerts and the destruction of buildings by bombing, with consequent overcrowding in other buildings. For example, although lectures were begun at 8 a m, by 10 a m there was usually an air-raid alert, which compelled students to enter shelters and remain there until noon. Frequently there was another alert at about 2 p m, evening study was interrupted by alerts, and sleep was constantly broken by alerts that came at about 2 00 a m. As a result of aerial warfare, not only was study and sleep interfered with, but only about half the time was it possible to attend classes. As the result of bombing of buildings, one of the professors of surgery had as many as 250 students in one class. Since the number of assistants decreased by one half and since the civilian patient load was quite heavy, it was impossible for the teachers to instruct the students as thoroughly as had been possible in peacetime.

### *Postgraduate Training*

In peacetime, the professors of medicine and surgery had approximately twenty to forty assistants, depending on the size of their clinics, but during the war the number was reduced by at least half. Assistants were appointed from a group of promising students who applied to the professor of their choice for postgraduate training in some specialty. If the applicant was an able-bodied man, he had to be deferred by the Army as nonessential and in addition had to be cleared by the Ministry of Education. The number of men available was so limited that it was necessary for the professors to accept an increasing number of women as assistants each year.

Assistants were paid from 5000 to 7000 marks yearly, depending on the length of service. At least one of them was used in the private clinic of the professor concerned for one year. Occasionally the professor would arrange for the assistant to increase his income by caring for semiprivate patients in the clinic and by filling out insurance reports and other papers. Health insurance appeared to be quite popular with the teaching staff.

In surgery, at least, a minimum of four years was required before the professor issued a certificate attesting that the assistant was qualified in his specialty. Assistants showing particular ability in teaching and research might be retained for as long as ten years. They were given more responsibility each year and were finally qualified for teaching appointments in the universities.

In peacetime and early in the war, at least two Army officers were sent to each clinic for further study in surgery and medicine. Before the end of the war the number of Army doctors sent and the time spent in the various clinics were variable. These men were assigned by the Army, and the number and type of students were no longer controlled by the professors.

not sealing the wound and of pushing rather than pulling its edges together. It gives better results with deep wounds than with shallow ones, in which it has a tendency to roll the edges inward. An extensive wound that laid the buttock open down to the sciatic notch and extended from the sacrum to the thigh was closed with wide adhesive "butter-fly" straps, with excellent healing and a completely satisfactory scar.

Closure has been accomplished largely with deep interrupted silk sutures, the bottom of the wound being picked up to obliterate dead space. Only rarely have buried sutures been used. If it is considered necessary to close the fascia of the thigh with buried catgut, a Penrose drain is inserted under the fascia and carried out through the most dependent portion. The drain is removed in forty-eight hours. If necessary, the skin margins are unhesitatingly freed to facilitate approximation.

If the size, shape or location of the wound prohibits direct closure, some type of grafting is indicated. The indications and technic for these procedures require special consideration and will not be discussed herein, but the principle of early closure at

the time of the first dressing applies equally well to plastic procedures. In other words, the wound should be closed at the optimum time by whatever method is necessary—simple closure if feasible, a split-thickness graft if the difficulty is just a question of too much skin loss, or a pedicle graft for gouged-out wounds exposing vital structures. In some wounds a combination of all three methods is required.

\* \* \*

Whatever the method of closure, it never has so favorable a chance of success as when done at the first dressing by the end of the first week. Complete epithelialization at this time affords the best possible dressing, lessens the incidence of infection, obviates painful dressings, conserves material and reduces nursing care and, most important, improves the chances for a good functional result. The goal of the evacuation system should be to get these patients to a hospital in which their wounds can be closed by the end of the first week. Intermediate dressings en route should be discouraged unless they are absolutely necessary.

## MEDICAL EDUCATION AND PRACTICE IN GERMANY DURING THE WAR

COLONEL ROBERT M. ZOLLINGER, M.C., A.U.S.

**I**NFORMATION concerning medical education and practice in Germany has been scanty during World War II. Because of the past achievements of German medicine it was considered important, both for the present and for the future, to attempt to evaluate its status during the last five secretive years. Certainly the standards of medical and surgical care of the German soldier at the front were not impressive. Only after the defeat of his country was it possible to visit the medical centers responsible for the education of the German medical profession. The following recent impressions were gained after visiting the clinics of the professors of medicine and surgery in three prominent German medical schools.

### MEDICAL EDUCATION

#### *Source of Students*

The quality of any professional school is founded not only on the educational and research facilities offered but also on the caliber of the students themselves. All the professors of the medical schools visited agreed that the caliber of the students was far below the prewar level. They recognized this as an alarming situation and believed that it was due to the following factors:

The majority of the students came directly from the Army, and in many instances they had been actuated only by a desire to avoid the hardships and dangers of combat. Consequently, they had ex-

pressed a desire to study medicine and had therefore been released by the Army for such study. In most cases they had neither the background nor the aptitude for study in a medical school. The students in this group consisted of physically fit men who were part of the so-called "Student Combatant Corps." They were under the direction of an Army officer in each school. They wore uniforms and were committed to the Army while at school and at the end of their studies. Their tuition was apparently paid by the State.

A smaller group consisted of soldiers discharged from the services because of general physical disability or for various other reasons. The State paid for their education and directed their assignment to a civilian or static military hospital after the completion of their education.

Another group consisted of those initially unfit for military service and of a few who had been excused from it because they had demonstrated a particular aptitude for the study of medicine. These students paid their own tuition, which amounted to 300 to 400 marks yearly, and their living expenses, which approximated 120 marks monthly. After completion of their studies, they were assigned to civilian or static military hospitals. A select few were trained as specialists following graduation.

The last group consisted of an increasing number of women who were admitted to the universities to

It was mentioned by a certain surgeon that one of the greatest advances in neurosurgery was the primary closure of compound wounds of the brain. Apparently primary suture of severed nerves at the time of injury was not practiced, but there was an attempt at loose approximation with one or more silk guide sutures. Secondary suture for injuries of the radial and ulnar nerves below the elbow was done four months after injury; that for nerve injuries above the elbow six months after injury, and that for division of the sciatic nerve eight months after injury. Early anastomosis of the nerve was not practiced, although it was generally agreed that better results might be obtained if early suture were attempted and if neurolysis were carried out more frequently.

The treatment of chest wounds was neither standardized nor modern in its concepts. Foreign bodies with rough edges larger than 1.5 cm in diameter were sometimes removed. Smooth asymptomatic foreign bodies were not removed unless there was associated hemorrhage, abscess or pain. Hemothorax was treated by occasional aspirations during the first four weeks, but no attempt was made to keep the pleural spaces completely dry. Decortication of the lung was not generally practiced, and it is probable that the indications for this operation were not understood. Empyemas were treated with constant suction for approximately three weeks through a No. 16 catheter; irrigations were not utilized during this period.

So far as could be determined, there were no new principles governing abdominal surgery; colostomies were not routinely performed for injuries to the large bowel. Sulfonamides were not applied within the intraperitoneal cavity unless there was evidence of established infection, but under such circumstances there was no hesitation in introducing as much as 20 gm of the drug.

Some attempts had been made to perform blood-vessel anastomosis, with fine silk as suture material. Heparin was apparently not available, and no special technics for anastomosis were developed. Occasionally the femoral vein was ligated as a prophylactic measure in the presence of pulmonary infarcts.

Extremely few early cases of trench foot had been treated in the civilian clinics visited. Those in charge were primarily concerned with the late complications, and invariably recommended paravertebral block of the lower two or three lumbar sympathetic ganglia, 10 cc. of 0.75 per cent novocain being used in each site. For troublesome causalgia, 1 cc of 70 per cent alcohol was injected in the vicinity of the appropriate ganglion after the preliminary injection of novocain.

The surgeons used vitamin preparations, but did not have so much confidence in this form of therapy as did the internists. Information was volunteered that children with infections who had been treated

in relatively dark bombproof hospital pregnancy on as six months and had got little sunlight do about as well as did those treated to a high hospitals where plenty of sunshine was a lowering Vitamin K did not seem to be used extensively. Patients with intense jaundice were with calcium and blood transfusions.

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ref. 10

Although there was general agreement that widespread use of whole-blood transfusion constituted one of the major advances of the war, there was little evidence that the actual requirements of whole blood in the various surgical conditions were understood. Transfusion was largely effected by an antiquated direct method, although occasionally the citrate method was employed, neither glucose nor refrigeration seemed to have been in use as a preservative in civilian hospitals. Each city had a list of donors, usually workers in large nearby factories, so that whole blood was readily available. The donors were paid 25 marks for each transfusion (500 cc), and in addition were given extra coupons for food rations; these incentives were sufficient to ensure an adequate supply of donors at all times. Wet plasma was available, but neither the dosage of blood nor that of plasma appeared to be controlled by laboratory tests or to be based on previous scientific estimations of the requirements for any particular type of case. No information concerning the use of plasma substitutes was obtained.

The operating rooms in the various clinics did not contain a single modern anesthesia machine. It may be that some of these machines had been sent to the Army or stored outside the city for protection against bombing. It could not be determined, however, that the surgeons employed gas anesthesia, and they seem to have had little experience with intratracheal anesthesia. They used 0.5 to 1.0 per cent novocain for local anesthesia in many operations, and barbiturates were widely employed intravenously. Ether was used for inhalation anesthesia except in cases presenting pulmonary infection, in which chloroform was used. There was little mention of spinal anesthesia, which was certainly not used in surgery of the upper abdomen. Morphine, pantopon, dilaudid and scopolamine were utilized in various combinations.

No new instruments or modern devices were observed in any of the clinics visited. Some of the surgeons, however, were enthusiastic about the use of long metal rods that were introduced into the medullary canal in the treatment of fractures of the long bones, especially those of the femur. They did not employ scalpels with detachable blades. Sewing clamps of the von Petz type were available for gastric and intestinal surgery. In most clinics an electrocoagulation and a cutting unit were available. Casual observation tended to confirm the



## Research

It was evident that there was little opportunity for research, and as a result few significant contributions in this field were made during the war. Although the various professors appeared to be of high caliber, and had in the past carried out or supervised extensive research projects, this activity during the war was greatly curtailed by many factors. In the first place, as already mentioned, the number of assistants was decreased by half. The students were of such poor quality that few had either the time or the inclination to assist in research projects. In some instances the professors had served for long periods as consultants in the Army. On their return to civilian life they were burdened with a tremendous professional load of civilian patients and casualties from air raids. In some cases extensive damage had been done to the clinics and laboratories, which further impeded research. In some clinics all the surgery had been performed during the past eighteen months in bomb-proof, partially underground hospitals of limited space. There was also an understandable shortage of drugs and supplies for patients, let alone research projects. The majority of professors, however, attempted to continue their investigations pertaining to subjects that had interested them for years, but many times they were unable to publish their findings or to have reprints of their articles made because of the paper shortage, or because of arbitrary discriminations of one kind or another made by Nazi officials. Apparently the latter were especially active in curtailing the publication of articles pertaining to a medicohistorical subject.

It is fair to say that individually the professors expressed resentment of the occasional appointment by the Nazis of inferior men to head departments, although such interference was apparently limited to certain universities. Furthermore, they appreciated keenly the loss to the universities in the last few years of some men as a result of racial discrimination. Inquiry was made of each professor regarding what he considered to be the greatest advance made during the war, invariably the answer was, "The use of sulfonamides." Second in importance was the rather widespread use of whole-blood transfusion. Penicillin had never been made available.

## MEDICAL PRACTICE

### Surgery

Specific inquiry was made concerning the principles of therapy utilized for some of the more frequent general surgical conditions. The various specialties were not evaluated. Although the basic principles of good surgery appeared to be thoroughly understood, it was evident that many practices were years behind the times. Although the individual clinics may have standardized their procedures, there was little evidence given by the men

who had served as senior consultants in the Army that a systematic routine for the management of battle casualties was practiced.

Sulfonamide therapy was considered the greatest advance of the war, and many different varieties of the drug, comparable to those available in the United States, were utilized. Although enthusiastic, the surgeons did not have so much confidence in the sulfonamides as did the internists. Certainly, in two of the large clinics they were not sure of the value of sulfonamides when applied locally in open wounds. Apparently both in civilian practice and in the Army it was optional with the surgeon whether sulfonamides were dusted into wounds. They all emphasized that adequate surgery was more important than chemotherapy. Sulfonamides were used in the treatment of gas gangrene, but the surgeons had no confidence in their effectiveness.

All wounds were débrided if seen within forty-eight hours after the time of injury, and the majority were left open. The value of early secondary closure for most wounds was not appreciated. A few large wounds were secondarily closed from five to seven days after débridement, but this was not a routine procedure in either civilian or Army practice.

Gas-gangrene antitoxin was used in the Army for wounds in susceptible areas, such as those of the upper thigh. There was general agreement that adequate radical surgery was the only efficient method of preventing gas gangrene, as well as of treating it after infection had developed. Little confidence was expressed in gas-gangrene antitoxin or the sulfonamide drugs in the management of such cases.

Relatively little tetanus was seen in civilian practice, although there had been a noted increase during the last six months. There was a tendency to attribute this to the fact that the recently manufactured antitoxin was probably defective. Tetanus antitoxin seems to have been given to all wounded men, and tetanus toxoid was reserved for special troops. Once tetanus had developed, it was treated by the daily injection of antitoxin, either intravenously or intrathecally. Avertin was used to control muscle spasm.

The treatment of burns appeared to be fairly standardized in the several clinics visited. In most of them the wound was débrided by brushing and by the application of alcohol under general anesthesia. Following this, a powder, whose active principle was tannin, was applied and the area was covered with dry gauze. In some cases boric acid and vaseline — and in others cod-liver oil — were applied to the burned areas. There was a tendency to give whole-blood transfusions daily, plasma was given only as a substitute. Pressure dressings, immobilization, early skin grafting and the requirements of blood and plasma replacement were not appreciated.

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normal limits. The peaks, too, were normal except in rare cases. The two-hour levels during pregnancy were abnormally high in a large percentage of cases (81 per cent). For this reason, a high two-hour level cannot be considered diagnostic of diabetes during pregnancy. On the other hand, the three-hour level was normal during pregnancy with one exception and may thus be more properly used as a criterion. The incidence of high two-hour values persisted immediately after delivery but dropped sharply after the puerperium. These find-

ings indicate an adverse effect of pregnancy on carbohydrate metabolism.

Pregnancy glycosuria is probably due to a high alimentary hyperglycemia rather than to a lowering of the renal threshold.

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### MECKEL'S DIVERTICULUM\*

#### With Report of a Case of Intussusception Due to Its Invagination

WARREN G. ATWOOD, M.D.†

FALL RIVER, MASSACHUSETTS

THE presence of an appendage or diverticulum in the small intestine was observed by Lavater<sup>1</sup> as early as 1672. In 1700, Littré described a structure that was probably a true congenital diverticulum, but stated that the appendage lacked the usual muscular coats.<sup>2</sup> Both Ruysch and Mery recorded the phenomenon in 1701.<sup>3</sup> Ruysch was the first to name it "diverticulum," and his *Thesaurus Anatomicus* contains an illustration of this blind sac. Morgagni<sup>4</sup> in 1769 mentioned several cases of diverticulum of the ileum and suggested their embryologic origin, having previously noticed this type of diverticulum in geese. Sandifort<sup>5</sup> described a case of acute intestinal obstruction probably due to Meckel's diverticulum as early as 1793. But inasmuch as Meckel<sup>6</sup> was the first to give an extensive description of this structure, with an explanation of its origin and clinical importance, his name was given to this particular diverticulum of the ileum. He described it as an embryonic rest or remnant of the vitelline duct that had failed to become obliterated.

The earliest known case of an anatomic specimen of this appendage is that placed in the anatomical museum of St. Bartholomew's Hospital, London in 1846.<sup>7</sup> The ornithologist Elliot Coues mentions finding this abnormality in birds and explains the variability of the site along developmental lines.<sup>8</sup>

In 1933, Harkins<sup>9</sup> published a report of 160 cases collected from the literature and added 2 of his own. A number of authors<sup>9-19</sup> have reported cases since this date, but little additional information is to be obtained from these cases beyond Harkins's conclusions. After reviewing the literature, he stated that Meckel's diverticulum occurs in normal people in 13 per cent of cases and is three times as frequent in males as in females. Many authors claim that

75 per cent are found in males. Meckel's diverticulum is found in 2 to 3 per cent of all autopsies. Intestinal obstruction from this abnormality occurs in an extremely small percentage of cases—15 per cent according to Harkins, 3 per cent according to Richardson and 6 per cent according to Halsted and Lichtenstern.<sup>2</sup>

The obstruction may be brought about in any one of a number of ways. The obliterated omphalomesenteric duct in the form of a fibrous band may constrict the bowel. The tip of the diverticulum may attach itself to some point in the peritoneal cavity and act as a constricting band. A long, mobile diverticulum may tie a knot around a loop of free bowel, as in Dorling's<sup>20</sup> case, in which the ileum was thus involved. A long diverticulum—the average diverticulum according to Lamb<sup>21</sup> is 5 cm. long—may become adherent to the intestine or umbilicus and act as a band, causing strangulation or volvulus. The diverticulum may invaginate itself into the lumen of the bowel and start an intussusception, in which case a polyp is often present in the diverticulum. The first case of this sort was cited by Moroni<sup>22</sup> in 1898. A starting point may be the expulsion of a fecal mass or concretion from the lumen of the diverticulum into the intestine. The diverticulum becomes inverted and acts as a polyp, initiating an intussusception. The mesentery is usually dragged into the intussusception and the traction causes pain. McCann<sup>2</sup> states that to invert a Meckel's diverticulum must hang free. As a rule, there are secondary attachments to the intestine, mesentery or umbilicus. Peristalsis of the diverticulum itself may cause inversion with negative pressure exerted by the rapid flow of intestinal contents. Inflammation may cause swelling at the base of the diaphragm and inversion into the lumen of the intestine. The bowel attempts to expel it, and this causes bleeding and inversion of the mucosa and serosa.

\*From the Department of Surgery, Truesdale Hospital.  
†Chief of surgical staff, Truesdale Hospital.

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100 cc — in young

Figure 1 that many

present during pregnancy

of abnormally high two-hour  
Table 1 The highest percentage

Percentage of Patients with High Two-Hour Blood-Sugar Levels

PERIOD	PERCENTAGE
First trimester	29
Second trimester	52
Third trimester	45
Sometime during pregnancy	81
Immediately after delivery	47
Postpartum	15

of abnormal two-hour levels occurred in the second and third trimesters and after delivery. Occasional values were as high as 164 mg per 100 cc. Only 2 patients in the post-partum group had high levels, and these were just over the critical level — 121 and 127 mg, respectively.

All the three-hour levels were normal throughout pregnancy and the post-partum period, except for two high values in 1 case. The values in this case are given in Table 2. There was an extremely

TABLE 2 Results of Glucose-Tolerance Tests in a Single Case

PERIOD	FASTING LEVEL mg / 100 cc	PEAK LEVEL mg / 100 cc	2 HOUR LEVEL mg / 100 cc	3 HOUR LEVEL mg / 100 cc
Second trimester*	96	143	136	155
Third trimester	93	162	131	122
Immediately after delivery	88	161	147	110
Postpartum	90	160	97	105

\*Patient first seen in second trimester

high three-hour level — 155 mg — in the first test. This followed a lower two-hour level, which suggests a technical error. The next curve gave a three-hour level of 122 mg, which is just over the normal value. Subsequent curves were normal.

### DISCUSSION

The above data indicate that normal pregnancy exerts a deleterious effect on carbohydrate metabolism, as is shown by the distortion of the glucose-tolerance tests. Two-hour blood-sugar levels over 120 mg were extremely frequent, especially during and after the second trimester. These persisted after delivery but returned to normal several months post partum. It is during the second trimester that diabetes often appears and that pre-existing diabetes is made worse.<sup>3</sup> Obviously, if a high two-hour blood-sugar level is considered diagnostic of diabetes, many normal pregnant patients — 81 per

cent of this series — would be so diagnosed. On the other hand, all the three-hour levels during pregnancy were normal except for those in 1 patient in whom subsequent determinations during pregnancy were normal. It is apparent that diabetes should not be diagnosed during pregnancy except when the most stringent criteria are applied — a high fasting blood sugar (over 120 mg per 100 cc but preferably over 130 mg) or a high three-hour level (over 120 mg). Even then an occasional case may show a return to normal after the puerperium.

In regard to the question of glycosuria during pregnancy, it is of interest that of the 4 patients who showed large amounts of sugar in the urine during the glucose-tolerance test, all but 1 had high blood sugars — over 180 mg — at the time of the glycosuria. Figure 2 illustrates this fact. Glycosuria

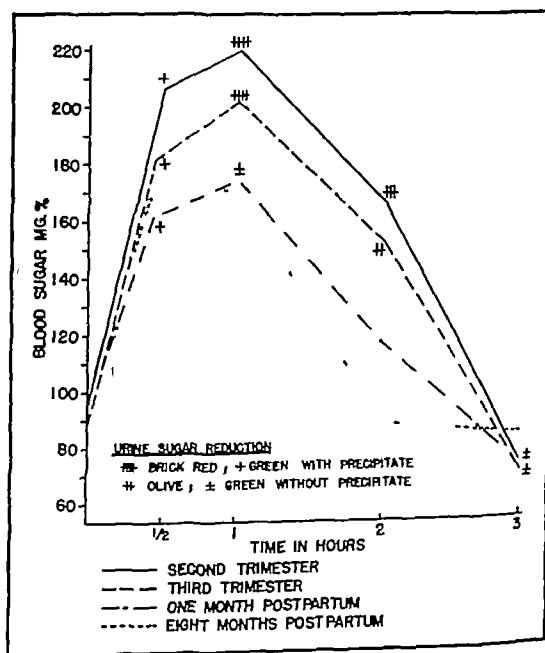


FIGURE 2 Glucose-Tolerance Curves on the Same Patient at Various Times during Pregnancy and after Delivery. Note the association of marked glycosuria with hyperglycemia.

during pregnancy is usually ascribed to lowering of the renal threshold. From this figure it is readily apparent that significant glycosuria occurred at the time of or soon after a marked elevation in the blood sugar. Since the curve dropped to normal, it is justifiable to classify these curves as those of high alimentary hyperglycemia.

### SUMMARY AND CONCLUSIONS

Serial glucose-tolerance tests were done on 25 normal pregnant patients — at each trimester, immediately after delivery and several months post partum.

The fasting blood-sugar values were well within

diverticulum On reduction of the intussusception, a dimple was found in the ileum at the point where the diverticulum inverted into the lumen of the bowel (Fig 1c) It was believed that a piece of green apple was the exciting cause of the intussusception No polyp was present

With considerable difficulty, the bowel was replaced in the abdominal cavity During this procedure the patient's condition caused anxiety Fluid was withdrawn from the stomach through a Levin tube The pulse was of poor quality and the skin color fair The patient's condition improved with the administration of oxygen and intravenous glucose No further operative measures were attempted The abdomen was closed with several mass interrupted nylon sutures through the peritoneum, muscle, fascia and skin

At the close of the operation, which lasted for 25 minutes the patient's condition was critical In spite of oxygen and supportive treatment, it became steadily worse, and death occurred 1 hour after operation Permission for an autopsy could not be obtained

In these cases a definite history of previous abdominal crises is fairly frequent In many there is a less severe attack a day or two before the final attack that sends the patient to the hospital One explanation is that the diverticulum becomes inverted before the bowel becomes invaginated

Colicky pain is present in almost every case reported Vomiting is present in 92 per cent of cases, and is a cardinal symptom out of proportion to other symptoms Tenderness and rigidity may not be present, even when the bowel is gangrenous A mass is almost always present, usually in the right lower quadrant of the abdomen The mass is rarely found palpable by rectum There is little fever or elevation of the white-cell count Melena may or may not be present The condition is usually taken for acute appendicitis or for intussusception from other causes Indications for operation are the same in both conditions, so that the differential diagnosis is of but academic interest

Harkins<sup>7</sup> states that the mortality in children is 56 per cent — 36 per cent in those over five years of age and 74 per cent in those under one year of age In many cases the diagnosis is made too late and operation is done only as a last resort when the pa-

dition and the diverticulum is not gangrenous, it should not be excised The intussusception may be treated by simple disinvagination Often, however, a one-stage or two-stage resection is necessary Bowel resection is less dangerous than it is in cases of ordinary intussusception, because most of the patients are older In Harkins's<sup>7</sup> series the average age was twenty-one years Bickham<sup>23</sup> advises excision

TABLE 2 Type of Operative Treatment

OPERATION	No of Cases
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of the diverticulum by a transverse elliptical incision, which should not be deep enough to result in encroachment on the lumen of the bowel The appendix should not be removed unless it is gangrenous or has thrombosed vessels When resection of the Meckel's diverticulum is considered feasible, a stricture may result from inversion with a purse-string suture After the diverticulum has been excised by a wedge-shaped incision, the intestine should be closed transversely to the long axis of the bowel Harris<sup>10</sup> makes an appeal to the surgeon to direct his mind from appendicitis in cases that are not clear cut In cases of this sort, if a simple appendectomy is performed, the patient is frequently again taken ill with an attack like the first one Furthermore, pain caused by a diverticulum is often considered to be due to adhesions, enteritis or colitis or the pelvic organs are blamed

## SUMMARY

The literature on the subject of intussusception due to an invaginated Meckel's diverticulum has been reviewed, and an additional case is reported On admission the cause of the obstruction presented a problem in diagnosis, which was revealed at laparotomy

The mechanism of the inversion of the Meckel's diverticulum to produce intussusception is illustrated

This case, which ended fatally, illustrates the need of early diagnosis and surgery, while the patient is still a good operative risk and also the need in any laparotomy of a search for a Meckel's diverticulum, especially in children

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tient is in extremely poor condition The benefit of early operation is seen in the statistics from his analysis of 160 cases (Table 1)

The treatment in the 24 operative cases at the Truesdale Hospital is shown in Table 2 In the case in which only appendectomy was done, the Meckel's diverticulum was noted, but it had a large base and was not excised The case in which cholecystectomy was done was complicated by a three-month pregnancy

Snigley,<sup>11</sup> who reports a series of 4 cases with recovery, states that if the patient is in poor con-

Meckel's diverticulum is usually found 30 to 45 cm proximal to the ileocecal valve, but it may occur at any point between the pylorus and the ileocecal valve — as a rule in the lower fourth of the ileum. Ordinarily it arises from the bowel opposite the attachment of the mesentery, but it may arise at either side or between the two leaves. In infants, it is often found nearer the ileocecal valve, because the site

Physical examination on admission showed a well developed, fairly well nourished, slender boy, complaining of severe abdominal pain. The lips were cyanotic, and the general condition was extremely poor. The temperature was 100.6°F, the pulse 130, and the respirations 22. The respirations were labored and slightly increased. There was a marked odor of acetone on the breath. The lungs were clear and resonant, and no rales were heard. The heart sounds were of fairly good quality, with a rapid rate. The abdomen was markedly distended and tympanitic to percussion, with generalized tenderness. No peristalsis was heard. The pa-

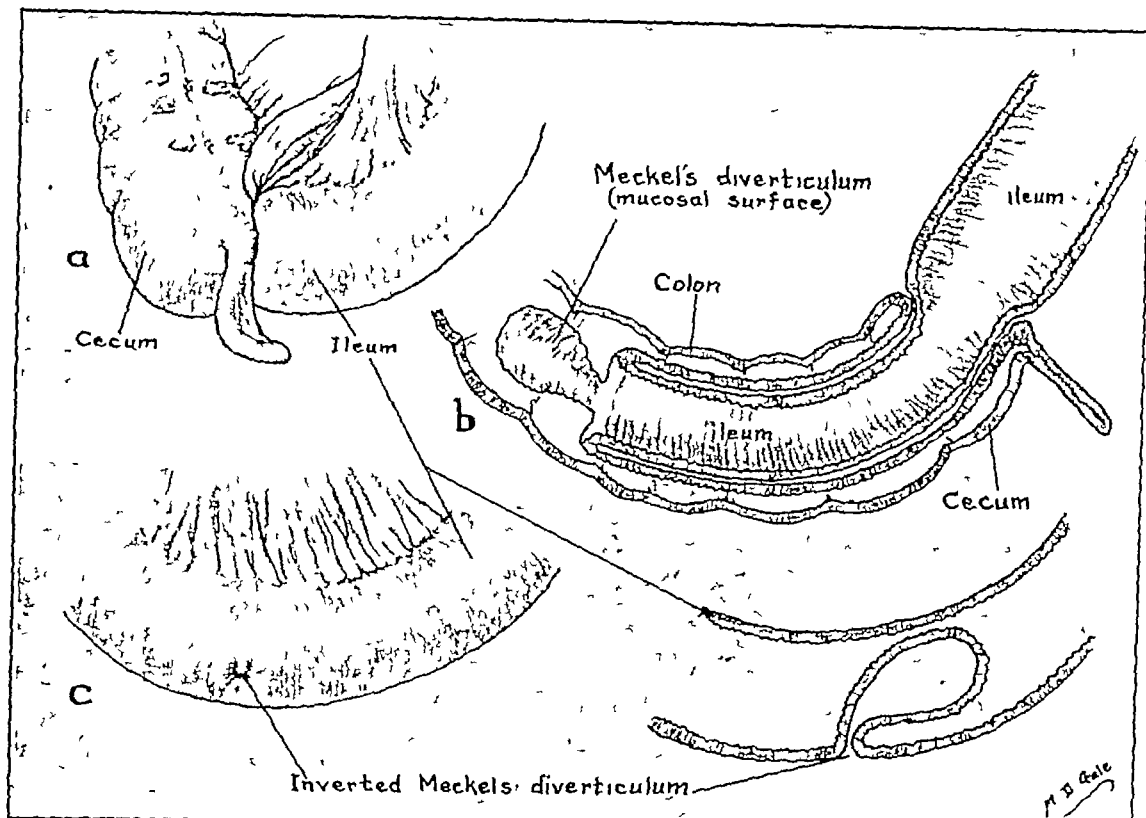


FIGURE 1

depends on the amount of growth in the portion of the intestine proximal to the insertion of the omphalovitelline duct.

Thirty-seven cases of Meckel's diverticulum have been recorded at the Truesdale Hospital in 69,000 admissions. Thirteen of these were found at autopsy. Intussusception as a result of inversion of the diverticulum occurred in only 1 case, which is reported below.

#### CASE REPORT

A S (65619), a 7-year-old boy, was admitted to the Truesdale Hospital on July 10, 1944. The mother stated that symptoms began on the morning of July 8, when the patient complained of severe abdominal pain, accompanied by nausea and vomiting. He had been eating green apples, and the mother thought that he had an ordinary stomachache. The pain continued during the following day, along with the nausea and vomiting. Early on the morning of July 10, the family physician was called. By that time the patient was lethargic and cyanotic. There was an odor of acidosis on the breath, and the abdomen was distended. He immediately referred the patient to the hospital. There was no history of any previous similar attack.

tient was thought to have acute intestinal obstruction from an unknown cause.

Urinalysis showed the slightest possible trace of albumin, large numbers of hyaline casts, a rare pus cell and mucus. The hemoglobin was 80 per cent, the red-cell count 4,440,000, and the white-cell count 14,650, with 69 per cent neutrophils, 20 per cent lymphocytes, 2 per cent large mononuclear leukocytes, 8 per cent band forms, and 1 per cent metamyelocytes.

The patient was extremely restless from the time of admission. The pulse was rapid and weak. He vomited at frequent intervals. A rectal tube was inserted, and 1000 cc. of 5 per cent glucose in saline solution was given by clysis.

At 2:20 p.m. the patient was taken to the operating room, where exploratory laparotomy was done under nitrous oxide, oxygen and ether anesthesia. The abdomen was opened through a right-rectus muscle-splitting incision. A considerable amount of foul-smelling fluid was present in the abdominal cavity. The small intestine was markedly distended and ballooned out of the abdomen. At that point, the patient vomited large quantities of foul-smelling fluid, suction was used, with a reasonably good result. His condition, however, was only fair.

By following along the small intestine in the direction of the cecum, a point of obstruction was located in the terminal ileum that had prolapsed through the ileocecal valve (Fig. 1a). The mechanism of the inversion and intussusception is shown in Figure 1b. The intussusception was reduced by expulsion and milking. At its apex was an inverted Meckel's

diverticulum On reduction of the intussusception, a dimple was found in the ileum at the point where the diverticulum inverted into the lumen of the bowel (Fig 1c) It was believed that a piece of green apple was the exciting cause of the intussusception No polyp was present

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## MEDICAL PROGRESS

### SYPHILIS

G MARSHALL CRAWFORD, M D \*

BOSTON

THE use of penicillin in syphilotherapy has become so widespread and the volume of literature regarding this drug so voluminous that this year's progress report on syphilis is being presented in slightly different fashion. A separate main division is devoted to penicillin and placed at the end of the report.

#### PUBLIC HEALTH

Little literature has appeared during the past year regarding the public-health aspects of syphilis. This may be due to some degree of optimism resulting from the remarkable reduction in the incidence of venereal disease during World War II. Never in history has any nation been able to accomplish such a feat. Despite this fact, control of venereal disease in the civilian population continues to be a tremendous problem. Editorial comment<sup>1</sup> cautions against overoptimism regarding its eradication. The recent advances in therapy, although highly effective, will not eliminate venereal disease unless more vigorous epidemiologic control is maintained. The establishment of rapid-treatment centers in many parts of the country, with the assistance of the United States Public Health Service through funds made available by Congress, is an example of what should now be done on a broader scale. By present methods of administration, penicillin treatment requires a week or more of hospitalization, and sufficient beds are not available. Syphilis must be dealt with in the same fashion as any other highly communicable disease, with the

co-operation of federal, state and local public health services, before the disease can be wiped out.

#### Incidence of Syphilis

Statistics are available on the incidence of syphilis in the first six months of the fiscal year 1944-1945, from the Health Officers' Monthly Statements.<sup>2</sup> The total amount of syphilis (171,535 cases) reported in the United States was approximately 25 per cent less than that reported during the first half of the preceding fiscal year. During the same period of time, primary and secondary syphilis (36,445 cases) continued to appear at nearly the same rate of incidence as in the year before. The latter figure indicates that public-health control measures have been holding the incidence of new infections about stationary. The decrease in total syphilis reported suggests that the reservoir of old infections is gradually being brought under treatment. If this is true, there should be a decrease in the amount of late crippling disease encountered hereafter.

The results of the first statutory requirement for mass civilian blood testing are now available. In July, 1943, the Legislature of Alabama passed a law requiring all civilians between the ages of fourteen and fifty to have their blood examined for syphilis. In the first three counties surveyed,<sup>3</sup> it was found that 80 to 90 per cent of the population voluntarily appeared to be tested, indicating that law-enforcement agencies will have to play but little part in the program. The Whites showed 2.2 per cent positive tests, and the Negroes 20.5 per cent. This is the commencement of an ideal campaign to eradicate syphilis. It will be time-consuming and expensive, but if continued on a nation-wide basis

\*Instructor in dermatology Harvard Medical School assistant dermatologist, Massachusetts General Hospital

may well constitute one of the greatest single public-health measures in history

### *Control Measures*

A summary of the contribution of the military forces toward postwar control of venereal disease<sup>4</sup> indicates a number of advantages that should greatly benefit the civilian population. A tremendous number of physicians and lay personnel trained by and educated in the military services regarding the principles of venereal-disease control will return to civilian life and will be available as workers in connection with venereal-disease control programs. Several million men who have received intensive venereal-disease education will return and should raise the level of information among the general public. Mass wartime experiences with the remarkable advances in treatment have contributed greatly to the therapeutic armamentarium. These factors present an unusual opportunity to reduce the incidence of venereal infection to a more readily controllable minimum.

The growth of programs for the control of venereal disease in industry is an encouraging circumstance. Anderson<sup>5</sup> has surveyed the accomplishments in this field, pointing out the co-operative achievements by both labor and management, and outlines the basic principles set down for the management of syphilis in industry by the United States Public Health Service. Industrial physicians, by following the medical objectives of an industrial venereal-disease control program and co-operating with state and local health departments, can be of great service in establishing intelligent control measures.

An analysis of case-finding measures<sup>6</sup> in venereal-disease control indicates that in the area surveyed more persons with infectious lesions voluntarily applied for aid than were brought under care by any other means. This illustrates the value of community education and of publicizing the availability of services. Although mass blood testing on a large enough scale will uncover more syphilis than will any other method of case finding, it will be severely handicapped unless intensive community education is successfully carried out.

An interesting report<sup>7</sup> on the value of educational procedures among the general public has appeared. A county in Georgia with a population of approximately 40,000, half being Negroes, was selected. Adequate facilities for diagnosis and treatment were provided. The community was then made aware of the prevalence of venereal disease, the facilities available and the newer methods of therapy. Every measure was taken to encourage patients to seek examination, either by private physicians or at public clinics. It was found that of the patients who came voluntarily to public-treatment centers, 76 per cent were directed to the clinic by posters seen in public lavatories. Negro churches were

utilized to disseminate information on venereal disease. An effort was made to encourage teaching on venereal disease in the schools for Negroes. Both these measures also proved of value, especially from the standpoint of improvement in knowledge of venereal disease. This report is an example of what can be accomplished even among the least privileged citizens.

### *Cost of Syphilis*

Estimating with any accuracy the financial burden imposed yearly on the Nation by this single disease is probably a near impossibility. A study is available, however, on the economic cost of paresis.<sup>8</sup> The data were obtained from a survey of admissions to state, county, city, private and Veterans Administration hospitals. The annual direct cost to the taxpayer of maintaining paretics is over \$11,000,000. The loss of income to the paretic patients themselves is estimated at \$112,000,000 yearly for men alone. These figures are astounding, especially when one considers that paresis is only one of the late manifestations of syphilis and not the only cause of insanity due to the disease.

### EXPERIMENTAL STUDIES

Aside from the vast amount of research related to penicillin in the treatment of syphilis, the main field of study has been related to hepatic dysfunction during the chemotherapy of syphilis. One investigator in particular, Dr A. C. Ivy, has for many years made an intensive study of the physiology and diseases of the liver. The excretion of neoarsphenamine arsenic and Mapharsen arsenic in the bile of dogs with permanent bile fistulas has recently been investigated by Ivy and his co-workers.<sup>9</sup> It was found that 40 per cent of the arsenic in Mapharsen was recovered in the bile in forty-eight hours, whereas the same percentage from neoarsphenamine was recovered in seventy-two hours. The production of choleresis in dogs did not augment the rate of excretion of arsenic in bile, and arsenic excreted in the bile was not thoroughly absorbed from the intestine. The administration of sodium dehydrocholate tended to decrease the elimination of arsenic, and the administration of sodium glycocholate and taurocholate, which cause less choleresis, increased the elimination of arsenic in the bile. If the administration of dehydrocholic acid diminishes the hepatotoxic action of neoarsphenamine and Mapharsen, it apparently does not do so by increasing their excretion in the bile. It was thus concluded that these results obviously do not provide a clear and substantial rationale for the administration of bile acids with arsenicals. Further work by the same group of investigators<sup>10</sup> indicated that neoarsphenamine does not constantly depress the output of cholic acid in dogs with a permanent biliary fistula. Mapharsen did constantly depress this output in

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The results of the first statutory requirement for mass civilian blood testing are now available. In July, 1943, the Legislature of Alabama passed a law requiring all civilians between the ages of fourteen and fifty to have their blood examined for syphilis. In the first three counties surveyed,<sup>3</sup> it was found that 80 to 90 per cent of the population voluntarily appeared to be tested, indicating that law-enforcement agencies will have to play but little part in the program. The Whites showed 2.2 per cent positive tests, and the Negroes 20.5 per cent. This is the commencement of an ideal campaign to eradicate syphilis. It will be time-consuming and expensive, but if continued on a nation-wide basis

\*Instructor in dermatology, Harvard Medical School; assistant dermatologist, Massachusetts General Hospital.

such reactions have been reported. Such diseases have been listed in these columns several times in recent years and will not be repeated at this time. It seems altogether possible that some of the diseases that Davis includes may not have been responsible for the false-positive reactions, since their incidences are so extremely low. Serologic tests for syphilis are subject to marked variations in sensitivity, which may account for a large proportion of discrepancies in published reports of false-positive reactions in various diseases. Technical errors also must not be forgotten. Davis stresses the importance of a sufficient period of observation, except during pregnancy, before making a final diagnosis in questionable cases. He indicates a period of three months, but a much longer time is often necessary. A point that is stressed is that a positive serologic test for syphilis is not an emergency. This is obviously true in the absence of infectious lesions, but neither should positive tests be lightly regarded, as so often occurs. Even the best trained men in other fields of work, from time to time, pay too little attention to positive serologic tests for syphilis and do not seek expert advice until the development of clinical lesions. These may be of minor clinical import, but they are not infrequently most distressing to the patient and are completely unnecessary.

Numerous reports on the effect of malaria on serologic tests for syphilis continue to appear. In a series of more than eight thousand tests carried out by six standard techniques, the Hinton flocculation test for syphilis showed the smallest proportion of false-positive reactions in malaria of any of the serologic techniques employed.<sup>22</sup> It was stated that in the absence of continued evidence of malarial infection, the persistence of positive reactions to any serologic test beyond a period of six weeks should arouse the suspicion of syphilis. This is a shorter time period than some observers have reported in the past, but agreement with a six-week time factor is available.<sup>23, 24</sup> Spinal-fluid examinations made on 100 malaria patients within forty-eight hours after hospitalization were found to be essentially normal.<sup>24</sup> Slight deviations from normal occurred in the spinal-fluid findings of 4 cases, but these were not indicative of syphilis and there were no neurologic symptoms.

Favorite<sup>25</sup> has continued his study of false-positive reactions for syphilis due to smallpox vaccination (vaccinia). Five hundred and twenty-five cases are included in his latest report. Of 202 patients on whom a single blood examination was performed, 11.8 per cent gave positive reactions. These appeared within two weeks of the date of vaccination and usually disappeared within two months, but a few weakly positive reactions persisted for as long as four months. A second group of 323 persons, who had had smallpox vaccinations several months previously, were given typhoid vaccine and tetanus toxoid to determine the role played by immuniza-

tion. No significant bearing on the production of false-positive serologic reactions for syphilis was observed. Recently vaccinated persons who had exhibited a temporary false-positive reaction did not have a reactivation of the reaction following typhoid and tetanus immunizations. It was found, however, that if these patients were revaccinated for smallpox within seven months, they might again present a weak serologic false-positive response for syphilis, even though the second vaccinia reaction was of the immune type. In a series of 129 patients with vaccinia reported during the past year, 44.9 per cent showed falsely doubtful or positive tests with one or more serodiagnostic procedures.<sup>26</sup> This is an extremely high incidence compared with that in most reports in the literature. The application of the Kahn verification test to post-vaccination false-positive serologic reports has apparently been useful.<sup>27</sup>

In contrast to Favorite's<sup>25</sup> experience with tetanus toxoid, other observers<sup>28</sup> report 8 cases in which biologic false-positive serologic reactions were considered to be directly related to stimulating doses of tetanus toxoid. Infectious hepatitis was apparently responsible for fifteen false-positive or doubtful serologic reactions after the clinical appearance of jaundice in 63 patients among allied military personnel in Sicily.<sup>29</sup> All but one of the reactions were negative by the seventh week. During an epidemic of upper respiratory infections among troops in this country, 100 patients were found to have positive serologic reactions for syphilis.<sup>30</sup> All had received routine Army immunizations from five days to four months previously. In 90 per cent of these cases, the false-positive nature of the serologic reactions was established. That the upper respiratory infection played any appreciable role in these false-positive cases seems doubtful.

### CLINICAL PROBLEMS

The third edition of *Modern Clinical Syphilology*, by Stokes,<sup>31</sup> appeared some months ago. This superb book on the diagnosis and treatment of syphilis has been brought up to date by the rewriting of a large proportion of the text and the addition of chapters on penicillin, military medicine and public health. Stokes's favorite and effective "thumbnail summaries" are featured as before. This magnificent work should be in the possession of everyone who is interested in syphilis.

### Reinfection

On numerous occasions in the past, the criteria for the cure of syphilis and for the diagnosis of reinfection with the disease have been discussed in these columns. The advent of intensive treatment programs and more lately the startling effectiveness of penicillin have necessarily brought about changes in the concept of such reinfection. It becomes increasingly difficult to differentiate relapse and re-

such dogs when the animals were deprived of bile acids. The oral administration of dehydrocholic acid may assist in counteracting the hepatotoxic action of Mapharsen. These findings led to the suggestion that patients scheduled to receive intensive arsenotherapy should for two or three days prior to the initiation of therapy have a liver-function test and be given a diet known to affect favorably the liver's resistance to poisons. Adequate protein is the essential feature of this diet.<sup>11</sup> Other workers,<sup>12</sup> studying liver damage from Mapharsen in dogs, present evidence that the oral administration of methionine affords protection against hepatic injury following large doses of Mapharsen given to protein-depleted dogs. Clinical application of this work indicates that the oral administration of methionine and cystine are effective in delaying the onset of liver damage and in diminishing the severity of the hepatitis in human beings treated with neoarsphenamine, but has no effect on the total incidence of liver damage.<sup>13</sup>

It is obvious from the reports of these several groups of investigators that the hepatotoxic effect of organic arsenical compounds is not too well understood. Present indications are that less and less arsenic will be used hereafter, if penicillin proves to be all that is hoped. It seems unlikely, however, that a form of chemotherapy that has stood so well the test of time can be completely discarded, and it is to be hoped that further study of these drugs will be continued.

### SEROLOGIC PROBLEMS

Considerable attention has been devoted during the past year to the blood serologic aspects of syphilis. There is a continuous striving to improve technic in the performance of blood tests and to eliminate the false-positive findings that are not infrequently encountered. But few of the reports in this field will be quoted, since much of the literature is of no direct value to the practicing physician. An excellent general discussion of the serologic findings in early syphilis is available.<sup>14</sup> It is pointed out therein that a limited serologic routine furnishes sufficient data for the usual diagnostic purposes and for the evaluation of clinical response to an established treatment. This justifies the performance of only one or two reliable tests, as carried out by most hospitals, state health departments and city laboratories.

The more highly refined quantitative tests are mainly valuable in gauging serologic response, such as a decreasing titer or the development of a serologic relapse. Their usefulness is thus limited to certain special situations and research projects. An extensive battery of different tests falls in the same category. Kahn<sup>15</sup> has published a short bulletin intended to serve as a practical guide to the technics of the various serologic tests that he has devised for the examination of serum and of spinal fluid.

The bulletin also outlines the method of interpreting and reporting these tests. This is a useful manual, especially for those engaged in laboratory work.

The indications for quantitative serologic tests for syphilis were reviewed in this journal some months ago.<sup>16</sup> Briefly enumerated, these include the diagnosis of primary syphilis in dark-field-negative lesions, comparative reagin titers in mother and child when congenital syphilis is suspected and the detection of impending relapse, including the clarification of certain technical points. Quantitative procedures estimate the potency (amount of reagin), in the same general fashion as in the Widal reaction, by quantitative titration of the serums. Some authors<sup>17</sup> advocate general adoption of these procedures for use in the management of every phase of syphilis. Limitations of their usefulness, possible difficulties of interpretation in general practice and the expense involved seem to preclude their widespread application at the present time.

Still further refinements in serologic technics are the verification tests that have been devised to assist in identifying false-positive serologic reactions. After extensive experience, Rein and Callender<sup>18</sup> believe that the average serologist is not able to distinguish consistently between true-positive and false-positive reactions by the use of any verifying test yet devised. They consider these tests, for the present, in the experimental stage and stress the oft-repeated caution that a diagnosis of syphilis should not depend on serologic reactions alone. The ensemble of available data, before diagnosis, should include the history and physical examination, radiologic studies, spinal-fluid findings and examination of contacts and family, in addition to repeated serologic reports from more than one laboratory. Additional measures may be necessary to rule out nonsyphilitic diseases that may cause false-positive serologic reactions. A discussion of the principles of verification tests is available,<sup>19</sup> with a description of the chemical and immunologic aspects of the reactions of syphilitic and false-positive serums. The possibility of the application of verification tests to the development of a practical method of differentiation is encouraging.

### False-Positive Reactions

General considerations on the occurrence of false-positive reactions for syphilis have been reviewed by Rein and Elsberg.<sup>20</sup> Most of this report is concerned with the so-called "biologic" false-positive reactions, occurring in such disease as vaccinia, upper respiratory infections, filariasis, Weil's disease, malaria, typhus fever and leprosy. The incidences of false-positive reactions in these diseases varied from 11.3 per cent in filariasis to 85.0 per cent in leprosy. Davis<sup>21</sup> reports a review of the literature regarding false-positive reactions for the years 1930-1943. He outlines the long list of diseases in which

such reactions have been reported. Such diseases have been listed in these columns several times in recent years and will not be repeated at this time. It seems altogether possible that some of the diseases that Davis includes may not have been responsible for the false-positive reactions, since their incidences are so extremely low. Serologic tests for syphilis are subject to marked variations in sensitivity, which may account for a large proportion of discrepancies in published reports of false-positive reactions in various diseases. Technical errors also must not be forgotten. Davis stresses the importance of a sufficient period of observation, except during pregnancy, before making a final diagnosis in questionable cases. He indicates a period of three months, but a much longer time is often necessary. A point that is stressed is that a positive serologic test for syphilis is not an emergency. This is obviously true in the absence of infectious lesions, but neither should positive tests be lightly regarded, as so often occurs. Even the best trained men in other fields of work, from time to time, pay too little attention to positive serologic tests for syphilis and do not seek expert advice until the development of clinical lesions. These may be of minor clinical import, but they are not infrequently most distressing to the patient and are completely unnecessary.

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**infection** The possibility of superinfection although less likely, should always be kept in mind. Cases of supposed reinfection are five to ten times as frequent as in previous years.<sup>32</sup> The difficulty of adequately differentiating reinfection and relapse is illustrated by the variety of criteria that can be found postulated in the literature. The simplest criteria merely require proof of syphilis prior to the occurrence of the supposed second infection. This proof must consist of demonstration of spirochetes in the lesion or the occurrence of a positive blood serologic test and should not depend on clinical judgment alone. After an interval following anti-syphilitic treatment, and at a site other than that of the primary lesion of the first infection, there must develop a new lesion with the characteristics of a chancre and in which spirochetes can be demonstrated. From these simplest criteria, one can go to the opposite extreme of the seventeen complex criteria that are proposed by Stokes. In some diseases, reinfection can be considered a proof of cure of a preceding infection. Moore<sup>32</sup> points out that this is not tenable with syphilis in human beings. After discussing the criteria of reinfection at some length, he states this opinion that, at the present time, re-infection cannot be differentiated from relapse on any grounds on which two or more observers would agree. He believes that this differentiation must rest on clinical impressions. This does not constitute proof. Moore points out that until order is brought out of the present confusion, all supposed reinfections must be regarded as treatment failures. This is especially applicable to the evaluation of new drugs and new treatment programs.

### *Syphilis of the Mouth*

The various forms of syphilis of the mouth are discussed in some detail by Wilson, Dunning and Fox.<sup>33</sup> It is pointed out that the dentist has a large responsibility in discovering oral manifestations of systemic diseases. The oral lesions of primary, secondary and late syphilis, both acquired and congenital, are described, including those of the lips, tongue, oral cavity, teeth and palate. A differentiation from the usual nonsyphilitic diseases that may simulate syphilis of the mouth is given. Included in this list are aphthous stomatitis, herpes simplex, herpes zoster, pemphigus, erythema multiforme, lichen planus, lupus erythematosus, leukoplakia, lupus vulgaris, Vincent's infection, granuloma pyogenicum, epithelioma, lingua plicata, lingua geographica, dysvitaminosis, hypovitaminosis, avitaminosis, pellagra, fungous infections and perlèche. A word of caution has been written against overlooking the possibility of cancer of the tongue in patients with syphilis.<sup>34</sup> It is pointed out that cancer can exist in conjunction with syphilis of the tongue in any stage, but may be overshadowed by syphilis when the cancer is early. More frequent

biopsies of possibly suspicious areas would provide an earlier diagnosis of cancer and a greater percentage of cures. Needless to say, adequate treatment for coexisting syphilis must be diligently pursued.

### *Visceral Syphilis*

O'Leary and Ockuly<sup>35</sup> point out that the only satisfactory method for determining that a lung lesion is syphilitic is a therapeutic test. The symptoms, physical signs and radiologic appearance of pulmonary syphilis are nondistinctive. When, however, a patient with positive serologic reactions is dyspneic, coughs, raises bloody sputum, has chest pain, is weak and loses weight and when physical and radiologic examinations indicate a nodular or infiltrative pulmonary process, one may presume that the lung lesion is syphilitic. If these signs and symptoms disappear after a course of therapy and do not recur, the opinion that the condition was syphilitic is tenable. In a series of 60 patients at the Mayo Clinic in which syphilis of the lung was considered a possibility, this diagnosis was substantiated in only 4 cases. Syphilis of the lung rarely recurs following involution under treatment.

Among 1705 consecutive adults admitted to a tuberculosis sanatorium for Negroes, 29.7 per cent were found to have positive serologic reactions for syphilis.<sup>36</sup> These patients were studied from a number of viewpoints without significant findings regarding a biologic relation between the two diseases. It has long been believed that the prognosis in such circumstances depends entirely on the tuberculosis, an opinion that was substantiated by this investigation.

Syphilis in diabetes has been studied by Perkin<sup>37</sup> over a five-year period. Among 550 diabetic patients comprising the series, 54 possible cases of syphilis (9.8 per cent) were found. The diabetes in the syphilitic group tended to be unusually mild. It is the author's opinion that syphilis, as well as all other so-called "causes" of diabetes, is merely a precipitating factor in the potential diabetic patient. These cases were observed for varying periods up to twelve years for changes in diabetic status. It is stated that there is some relation between latent syphilis in the diabetic patient and the occurrence of gangrene, but the supporting evidence is not too conclusive.

### *Neurosyphilis*

An interesting study concerns the incidence of asymptomatic neurosyphilis in young men.<sup>38</sup> The data were obtained from the spinal-fluid findings of 3000 syphilitic military selectees passing through an induction station. Sufficient pathologic changes to cause rejection were found in 294 (9.5 per cent), all but 15 of whom had positive Wassermann reactions in the spinal fluid. The second most frequent abnormality was an increased globulin (174 cases). The colloidal gold curve was elevated in 92 cases,

but only 38 of the 3000 spinal fluids showed an increase in cell count

A strikingly low percentage of lumbar-puncture headaches were observed in an army camp<sup>39</sup> During a five-month period, lumbar punctures were performed on 2217 syphilitic patients, among whom only 15 (less than 1 per cent) developed post-puncture headache severe enough to require bed rest The fluids were collected rapidly, the patients immediately got on their feet and were instructed to keep active and not to lie down It was believed that more nearly normal intracranial pressure was maintained by the erect position, thus preventing oversecretion and compensatory hypertension, with resultant headache

An excellent review and clinical survey of symptomatic neurosyphilis has been published by Solomon, Moore, O'Leary, Stokes and Thomas<sup>40</sup> It is pointed out that the symptoms of syphilis of the nervous system may simulate all forms and varieties of neuropsychiatric disorder Obviously, then in any disorder suggesting organic involvement of the nervous system neurosyphilis must be ruled out These authors divide neurosyphilis into two main categories meningovascular neurosyphilis, which produces little or no irreparable damage to nerve cells, except secondarily by interruption of the blood supply, and parenchymatous neurosyphilis Trivalent arsenicals and bismuth are of great benefit in meningovascular disease but not in parenchymatous neurosyphilis Obviously, the clinical distinction between the two is of great importance The symptoms of neurosyphilis are directly dependent on the site of involvement as well as on the extent of the lesion The clinical manifestations of the various types of neurosyphilis — syphilitic meningitis, meningovascular neurosyphilis, tabes dorsalis, general paresis, vascular neurosyphilis and congenital neurosyphilis — are described Tabes dorsalis and its sequelae are discussed at some length The great variety of symptoms that may be due to general paresis are emphasized Attention is directed to the fact that early stages of dementia paralytica are too easily and too frequently confused with psychoneurosis The treatment of each variety of neurosyphilis is discussed It is well known that parenchymatous neurosyphilis may be accompanied by negative spinal-fluid findings Seven cases of general paresis were recently reported in which a negative spinal-fluid Wassermann reaction<sup>41</sup> occurred Several of these patients exhibited completely negative spinal fluids

(To be concluded)

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biopsies of possibly suspicious areas would provide an earlier diagnosis of cancer and a greater percentage of cures. Needless to say, adequate treatment for coexisting syphilis must be diligently pursued.

### *Visceral Syphilis*

O'Leary and Ockuly<sup>35</sup> point out that the only satisfactory method for determining that a lung lesion is syphilitic is a therapeutic test. The symptoms, physical signs and radiologic appearance of pulmonary syphilis are nondistinctive. When, however, a patient with positive serologic reactions is dyspneic, coughs, raises bloody sputum, has chest pain, is weak and loses weight and when physical and radiologic examinations indicate a nodular or infiltrative pulmonary process, one may presume that the lung lesion is syphilitic. If these signs and symptoms disappear after a course of therapy and do not recur, the opinion that the condition was syphilitic is tenable. In a series of 60 patients at the Mayo Clinic in which syphilis of the lung was considered a possibility, this diagnosis was substantiated in only 4 cases. Syphilis of the lung rarely recurs following involution under treatment.

Among 1705 consecutive adults admitted to a tuberculosis sanatorium for Negroes, 29.7 per cent were found to have positive serologic reactions for syphilis.<sup>36</sup> These patients were studied from a number of viewpoints without significant findings regarding a biologic relation between the two diseases. It has long been believed that the prognosis in such circumstances depends entirely on the tuberculosis, an opinion that was substantiated by this investigation.

Syphilis in diabetes has been studied by Perkin<sup>37</sup> over a five-year period. Among 550 diabetic patients comprising the series, 54 possible cases of syphilis (9.8 per cent) were found. The diabetes in the syphilitic group tended to be unusually mild. It is the author's opinion that syphilis, as well as all other so-called "causes" of diabetes, is merely a precipitating factor in the potential diabetic patient. These cases were observed for varying periods up to twelve years for changes in diabetic status. It is stated that there is some relation between latent syphilis in the diabetic patient and the occurrence of gangrene, but the supporting evidence is not too conclusive.

### *Neurosyphilis*

An interesting study concerns the incidence of asymptomatic neurosyphilis in young men.<sup>38</sup> The data were obtained from the spinal-fluid findings of 3000 syphilitic military selectees passing through an induction station. Sufficient pathologic changes to cause rejection were found in 294 (9.5 per cent), all but 15 of whom had positive Wassermann reactions in the spinal fluid. The second most frequent abnormality was an increased globulin (174 cases). The colloidal gold curve was elevated in 92 cases,

3 Provision of adequate medical care for those unable to obtain it by voluntary prepayment plans or by direct payment is the responsibility of the local or state government. Part of the burden of this responsibility may be assumed by charitable agencies. Federal grants-in-aid to state programs administered by state boards of health is an acceptable method of helping to meet this responsibility.

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The committee recommends the adoption by the Council of the above basic principles as essential to the development of any successful medical-care plan and, as guides by which to evaluate medical-care plans that may be proposed in future, with the understanding that changing conditions may require their later revision.

Dr Root moved the adoption of this recommendation. This motion was seconded, and it was so ordered by vote of the Council.

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(1) The bill makes no adequate provision for general public-health programs that are more fundamental than this specialized legislation.

(2) Services and facilities are available to all who elect to participate, regardless of economic status. (This violates Basic Principles 4 and 5.)

(3) The public deserves a reasonable estimate concerning the ultimate cost of this proposed legislation. Experience and such factual data as are available indicate an ultimate annual budget approximating one billion dollars. This should be clearly recognized in any consideration of the bill.

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Title II makes provision for full medical, dental, nursing and laboratory care and hospitalization for those able to pay for such services.

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#### TITLE I GRANTS TO STATES FOR HEALTH SERVICES

##### Part A Grants to States for Public-Health Services

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We approve of federal grants to aid the several states in assuming their responsibility of providing medical care for those unable to pay for such services. We approve in general of this part of the bill as written with the following exceptions:

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32101

#### PRESENTATION OF CASE

*First admission* A sixty-five-year-old unemployed man entered the hospital because of a chronic draining ulcer of the lower lateral aspect of the right leg

He had first been seen in the Orthopedic Clinic thirty-two years previously for a partially healed fracture of the right tibia just above the ankle. At that time an arthroplasty was performed and a metal plate was applied to the fibula. The ankle functioned well until about a year before admission when a bruise developed over the right external malleolus after a minor injury. This gradually spread, and nine months later the skin broke down there was constant drainage from the area thereafter. In the five years prior to admission he was seen many times in the Medical Clinic for a variety of complaints. Early in this period he had an episode of weakness, unproductive cough and fever lasting six weeks. His temperature during that time averaged 101°F. There was no sweating. He was well for several months and then had an attack of "bronchitis," during which he had chills, a fever rising to 104°F and blood-streaked sputum for a period of three weeks. In addition to these febrile attacks he developed mild dyspnea on exertion and swelling of the ankles, most pronounced in the evening. At the same time he was troubled by difficulty in starting the urinary stream and by nocturia (one or two times). There were also numerous episodes of vague epigastric distress, with sensations of fullness and discomfort, sometimes accompanied by shortness of breath. X-ray examination of the chest at this hospital four years before admission showed clear lung fields. The cardiac pulsations were said to be extremely small. An electrocardiogram showed a PR interval of 0.16 second, a flat T<sub>1</sub>, inverted T<sub>2</sub> and T<sub>3</sub> and a low T<sub>4</sub>. The blood pressure on three occasions was 112 systolic, 90 diastolic, 100 systolic, 70 diastolic, and 80 systolic, 70 diastolic. The liver was palpable three fingerbreadths below the rib margin. He received 0.1 gm of digitalis daily during the

four-year period before admission, but continued to have episodes of ankle edema, swelling of the lower abdomen and dyspnea on moderate exertion. He stayed in bed for one to six weeks at times when these symptoms were at their worst.

Physical examination showed marked pigmentation and a 1-cm ulcer on the lateral aspect of the right fibula. The head of a screw was visible in the floor of the ulcer. There were scattered rales at the lung bases. The heart was normal.

The temperature was 97°F, the pulse 80, and the respirations 20. The blood pressure was 120 systolic, 88 diastolic.

An x-ray film of the ankle showed bone absorption and periosteal proliferation about the metal plate. The lower end was free in the soft tissues. A chest plate showed hazy density of the left lower lung field. The left leaf of the diaphragm could not be visualized. The heart was in transverse position and appeared slightly enlarged to the left. There was no change in the electrocardiographic findings from the previous examination.

The bone plate was removed, and the wound healed slowly. A thoracentesis on the left side yielded 35 cc of clear yellow fluid, which was negative for tumor cells, a guinea pig inoculated with it failed to develop tuberculosis.

*Second admission* (five months later) One month prior to this admission the patient developed pain in the left side of the chest, which persisted. It began at a point just below and lateral to the nipple and extended to a point just below the angle of the scapula. At first it was aggravated by deep respiration, but it was gradually reduced to a dull, constant ache. He lost 10 pounds in the month prior to entry. There was no cough or sensation of fever, although exertional dyspnea persisted.

On examination of the chest there were flatness and absent tactile fremitus and greatly diminished breath sounds over the lower half of the left chest. The temperature was 100°F.

Seven hundred and twenty cubic centimeters of bloody, cloudy fluid was removed through the ninth left intercostal space. The patient was discharged unimproved except that his temperature was normal on the fifth hospital day.

*Third admission* (six months later) The chest pain persisted after discharge except for periods of one to three days after each of four thoracenteses performed in the Emergency Ward. They yielded diminishing amounts of fluid, and after each a friction rub was heard. There had been no further weight loss, nor had cough or other symptoms developed.

The trachea was deviated slightly to the left. The first heart sound at the apex was slapping in character. The pulmonic second sound was split giving an apparent systolic gallop. The left side of the thorax was flatter than the right and moved

(1) We believe that all federal grants-in-aid for the medical care of needy persons should be made by the United States Public Health Service to state departments of public health until such time as these grants may be made by a federal Department of Public Health

(2) We disapprove of the provision that places the responsibility in the Social Security Board on the federal level and in the Department of Welfare on a state level (Section 131)

(3) This Society through its Blue Shield has approved of the service principle rather than the payment to patients of cash benefits for medical care. We disapprove of the provision in the bill of making cash payments to individuals for this purpose

#### TITLE II PREPAID PERSONAL HEALTH-SERVICE BENEFITS

This is compulsory health insurance. It would be very costly to carry out the provisions of this section of the bill, and there is nothing to intimate what this will add to the burden of the taxpayer or how the money will be raised. Since we believe that the payment for medical care of those able to pay for such services by direct payment or on a prepayment basis is the responsibility of the individual and that with the extension and development of voluntary prepayment or other plans particularly adapted to certain areas, medical care of the highest quality can be obtained at a reasonable cost, we disapprove of this section

\* \* \*

The Committee on Postwar Planning recommends that the Council direct the president of the Society to appoint a representative and an alternate to appear before the appropriate committees of the Congress of the United States for the purpose of making known the views of the

Massachusetts Medical Society with regard to the Wagner-Murray-Dingell Bill (Senate 1606) and the Maternal and Child Welfare Act of 1945 (Senate 1318)

Dr. Root moved the adoption of this recommendation. This motion was seconded, and it was so ordered by vote of the Council

The committee further recommends that the Council send copies of the article "Information on the Deliberations of the Subcommittee on Medical Economics," together with the action of the Council of the Massachusetts Medical Society, to all the members of the Congress of the United States, to the members of the Massachusetts Legislature and to the newspapers of the Commonwealth

Dr. Root moved the adoption of this recommendation. This motion was seconded, and it was so ordered by vote of the Council

It was moved by Dr. Leroy E. Parkins, Suffolk, and seconded, that the members of the various committees who had spent so many long hours of vigilant effort in preparing this report be given a vote of thanks. This motion was amended so as to include the President for his expert guidance. The motion was adopted by vote of the Council

The Council adjourned at 6:35 p.m.

MICHAEL A. TIGHE, *Secretary*

So far as the findings by x-ray are concerned there was what was called a thickened pleura, which persisted over a long period of time. The heart was displaced toward the affected side, and it looks as if there was some underlying lung condition, because they describe a partial collapse of the lower lobe.

So far as the heart is concerned there were dyspnea, cyanosis, edema of the ankles, a large liver and fluid in the abdomen. That concludes the story of his symptoms, but along with that we are given a good deal of information. They tell us that he had small cardiac pulsations, a low blood pressure, a low pulse pressure and electrocardiographic findings that, to my knowledge, are consistent with constrictive pericarditis. I do not see how one can get away from such a diagnosis. Except for the pericardial changes, I cannot see how the heart was involved. This man was sixty-five years old. I grant that that is above the average for constrictive pericarditis, but it can happen at that age.

Let us look at the lung films and guess as much as we can about the lung condition.

DR. MILFORD D. SCHULZ: The earliest chest film that I can find is a lateral view taken in 1943, three years before his death.

DR. KING: I think that it shows some involvement in the lung base.

DR. SCHULZ: I agree. In the 1944 films you can see collapse of the left lower lobe and some pleural deformity on each side. In those of 1945, there is a newly developed density described as being in the dorsal division of the lower lobe. I wonder, however, if it is not in the basal portion of the upper lobe.

DR. KING: All you can say is that he had partial collapse of the lower lobe and pleural involvement?

DR. SCHULZ: Yes. I am looking for calcification in the pericardium, but I do not see any.

DR. KING: These are the films on the last admission, when he came in with what I should say was an acute pneumococcal pneumonia, which I am going to add on top of the old process. He had plenty of Type 3 pneumococci in the throat, not actually in the sputum. Does that not look more like an acute pneumonic process than an infarct?

DR. SCHULZ: Yes. If it is an infarct, it is a big one.

DR. KING: Would you be willing to agree that these films are consistent with an acute pneumonia that later spread to the apex of the lung?

DR. SCHULZ: Yes, that is what I thought it was when I looked at it.

DR. KING: So far as the pleural process is concerned, I do not know of anything that will give a pleural reaction of this severity and duration and with fluid except tuberculosis. And if one accepts that diagnosis for the pleurisy, one had best accept it also for the pericarditis. The literature tells of constrictive pleuritis, as well as constrictive peri-

carditis, but there is no evidence of constrictive pleuritis here.

I realize that two pieces of evidence have been given that are against the diagnosis of tuberculosis—a negative guinea-pig inoculation of the chest fluid and a negative biopsy of the pleura. But 35 cc of fluid is too small an amount for satisfactory examination for tubercle bacilli, especially if one also looks for tumor cells, and although I am not sure of this, I believe that a tuberculous pleurisy may in certain areas show only collagenous tissue, with no definite tubercles. I realize, too, that when pericarditis and pleuritis occur together they are often idiopathic and are never adequately explained. Nevertheless I still hold to the diagnosis of tuberculosis of the pleura and pericardium.

The diagnosis of tuberculosis of the lung is still more difficult to substantiate, but I shall guess that there was tuberculosis in the partially collapsed lobe. It is also possible that at death there was considerable tuberculosis outside this area, but we have no proof of that. Apparently the sputum was not examined for tubercle bacilli—a too frequent oversight. I find that these days the first thought is for the chemical constituents, and sputum examination is often not thought of. Speaking of the chemical findings, the albumin-globulin ratio in this case is consistent with constrictive pericarditis.

Next there is the liver. Did he have cirrhosis? And was it a true Pick's disease—mediastino-pericarditic pseudo-cirrhosis of the liver? I suppose that that is what he had. Did he also have chronic peritonitis, which is frequent in these cases? Again, in a long-standing case of this sort I suppose that he did.

When he came to die, I think that he had a Type 3 pneumococcus pneumonia and that he died from a pulmonary embolus. I do not see how we can prove that he had infarcts in the lung, but I believe that he probably did have them.

All of which gives us a great many diagnoses, but I seem forced to take them all—tuberculous constrictive pericarditis, tuberculous pleurisy, pulmonary tuberculosis, pulmonary embolus (fatal), pulmonary infarcts, Type 3 pneumococcus pneumonia and "pseudo-cirrhosis of the liver."

DR. EDWARD F. BLAND: Is there any mention made of cervical veins?

DR. KING: I do not know why we are not given the venous pressure. It would be a help. Whether I can assume they were normal, I do not know.

I am interested to know if you would make a diagnosis of constrictive pericarditis, Dr. Bland?

DR. BLAND: I do not believe so.

DR. KING: Perhaps you know too much about the case.

DR. BLAND: No.

DR. ALBERT J. STUNKARD: The patient had no



poorly. The percussion note in the left axilla and lower half of the left chest was flat, breath sounds and tactile fremitus were diminished. The left side of the diaphragm did not appear to move. The liver was palpable two fingerbreadths below the ribs. X-ray examination revealed a markedly thickened pleura on the left side, with probable partial underlying collapse of the left lobe. The heart was displaced to the left, and there was a small amount of free fluid just above the diaphragm.

Biopsy of the left pleura showed slight chronic inflammation in dense collagenous tissue. Ten days after the operation he had a chill, with a rapid pulse and a temperature of 102°F, followed by a dry painful cough and pain on deep inspiration. There was slight ankle edema. No tenderness was elicited in the thighs or calves. The serum protein was 5.8 gm per 100 cc, with an albumin of 2.4 gm and a globulin of 3.4 gm. The prothrombin time was 28 seconds (normal, 22 seconds). The febrile episode lasted three days. He was discharged on the twenty-eighth hospital day.

*Fourth admission* (four months later). Soon after discharge the nocturia gradually increased so that he urinated every two hours. There were dribbling and some incontinence, followed by dysuria. The prostate was symmetrically enlarged to twice its normal size. A transurethral resection for benign prostatic hyperplasia was performed. Postoperatively he had an immediate episode of nervousness and shaking accompanied by cyanosis but without a chilly sensation, dyspnea or pain. The temperature rose to 104°F. This lasted only a few hours. He was discharged on the fifth postoperative day.

*Final admission* (two years later). He was apparently well until three days before re-entry, when he developed cough, with malaise and increasing fever.

On physical examination the lips were moderately cyanotic and the skin was flushed and hot. He was breathing hard at a rate of 40 respirations per minute. The right lung over the midportion posteriorly was dull to percussion, with bronchial breathing and inconstant rales in this area. The left cardiac border was 11 cm to the left of the mid-sternal line. The rhythm was irregular, and the rate rapid.

The red-cell count was 5,450,000, and the hemoglobin 16.9 gm. The white-cell count was 16,400, with 92 per cent neutrophils, band forms predominating. The urine had a specific gravity of 1.018 and gave a ++ test for albumin. The sediment contained 25 white cells and a rare red cell per high-power field.

The temperature was 104°F, and the pulse 120. The blood pressure was 100 systolic, 60 diastolic.

X-ray films revealed an area of increased density in the right upper lung field, probably located in the dorsal division of the lower lobe. There was also an ill defined density in the left lower lung

field, with apparent decrease in the size of the left lower lobe and also a line of density extending along the lateral chest wall.

The patient was started on penicillin (32,000 units every two hours). On the day after admission the temperature had fallen to 100°F and the respirations to 25. The patient felt better but was coughing up bloody sputum and had a pulse of 116, despite 0.8 mg of Cedilanid intravenously and 0.4 mg of Purodigin over a twelve-hour period. There was less dullness posteriorly but there were increased fine rales throughout most of the right chest. Abundant Type 3 pneumococci were isolated from the throat.

Two days later the temperature was back to 102°F and he still had rales and was coughing up blood-streaked sputum. Sulfadiazine was started in addition to penicillin. On the seventh hospital day he developed a generalized itching erythematous rash. There was considerable exfoliation over the arms. The pharynx was normal. Sulfadiazine was stopped. Subsequently, the rash improved but the patient's condition continued to deteriorate. He remained cyanotic. He developed shifting dullness in the abdomen, and the liver was palpable two fingerbreadths below the ribs. Rales and rhonchi were constant in all lung fields.

On the eighteenth hospital day, just after he had been taken off the bed pan, he gasped, fell back on the pillow deeply cyanotic and died.

#### DIFFERENTIAL DIAGNOSIS

DR DONALD S. KING. Four organs were involved in this long story: they took out a benign prostate, and then there were three. The prostate explains satisfactorily the urinary symptoms. The remaining involved areas are the leg—with the fracture many years before and the infection recently occurring around the bone plate—and the lungs and the heart, both of which had given symptoms for four years, long before the recurrence of symptoms in the leg. Of course, the temptation, when one is presented with this story, is to try to combine all three systems in one diagnosis and say that the chest symptoms were embolic phenomena, with the source in the infected area in the leg. But as we shall see, such an explanation is not sufficient to cover all the findings.

So far as the pulmonary symptoms are concerned, there were episodes of fever, and it was real fever, sometimes with chills. At times the high temperature persisted for as long as six weeks. One assumes that the fever came from the lung or the pleura. There was a cough, which was dry except for occasional bloody sputum, nothing is said about pus, foul or otherwise. Then there were attacks of definite pleural pain, which changed to an ache and persisted. Then there was fluid that took a long time to disappear. At one time the fluid was bloody, otherwise it was clear.

pain and was markedly constipated. There was no blood in the stools. Three days before admission, poorly localized abdominal pain again appeared, with pain in the rectum. During this three-day period he had no bowel movements. A few hours before admission he vomited a small amount on three occasions.

The past history revealed that the patient had been constipated for many years, using a laxative daily to obtain a normal bowel movement. For several years he had complained of progressively severer frequency, nocturia and urgency. A year and a half before this admission the prostate was found to be moderately enlarged. A transurethral resection was done, from which he recovered uneventfully.

Physical examination revealed a well developed and nourished man. The skin was warm and moist. The pupils were normal. The heart was not enlarged, and there were no murmurs. There were a few coarse rales at both lung bases. The abdomen was soft, and there was slight tenderness in both lower quadrants. Peristalsis was normal. The prostate was small. The reflexes were normal.

Temperature was 100°F, the pulse 100, and the respirations 25. The blood pressure was 160 systolic, 85 diastolic.

The hemoglobin was 85 per cent. The white-cell count was 14,000. The urine was normal. The nonprotein nitrogen was 31 mg per 100 cc. The total serum protein was 5.8 gm per 100 cc, and the chloride 90 milliequiv per liter. The blood Hinton reaction was negative.

A flat film of the abdomen showed a large amount of gas and retained bowel contents in the large bowel without evidence of obstruction. Several loops of large bowel were dilated. The bones of the lumbar spine showed advanced hypertrophic changes.

A barium enema shortly after admission showed numerous diverticulums of the sigmoid. No spasm was observed fluoroscopically. The bowel wall in this area was irregular. The terminal ileum was not visualized. Shortly after the barium enema had been given, the abdomen was noted to be tense and boardlike, with absent peristalsis, and tenderness became generalized.

About two hours later a plain film showed the greater portion of the barium to be retained in the large bowel. A film with the patient standing showed no evidence of air beneath the diaphragm.

An immediate exploratory laparotomy was done.

#### DIFFERENTIAL DIAGNOSIS

DR. FIORINDO A. SIMEONE This is the case of a seventy-eight-year-old man who had a lesion which caused partial obstruction of the large intestine and developed a complication necessitating an emergency operation. There is no supporting evidence that the final episode of abdominal spasm and tenderness could have been due to "abdominal apo-

plexy" or to volvulus and strangulation. These possibilities are therefore dismissed, and I believe that it is reasonable to explain the present illness and the final episode on the basis of a single lesion.

One has to decide whether the lesion causing partial obstruction was intrinsic or extrinsic relative to the bowel. The patient had a history of mild urinary-tract obstruction, which might have been due to cancer of the prostate, but this was apparently cured by transurethral resection and there is no evidence of recurrence. Rectal examination on entry showed a normal prostate, and nothing is recorded to suggest a pelvic mass that could have caused obstruction of the large intestine from extrinsic pressure. The roentgenograph apparently did not suggest adynamic ileus, and the negative Hinton reaction rules out the adynamic ileus occasionally seen in *tabes dorsalis*.

We are thus left with a lesion that was probably intrinsic in the large intestine and certainly interfered mechanically with the normal emptying of the bowel. Five important lesions are to be considered in the differential diagnosis of large-bowel obstruction in a man of seventy-eight — malignant tumor, diverticulitis, hernia, volvulus and appendiceal abscess. The lack of signs in the right lower quadrant, the failure to demonstrate a mass and the localization of the nonspastic lesion in the sigmoid by roentgenograph are sufficient to rule out appendicitis with abscess formation. Physical examination and the x-ray findings rule out hernia and volvulus. It remains, therefore, to distinguish between diverticulitis and carcinoma of the sigmoid. Tumors of mesodermal origin in the wall of the large bowel are not considered because they are rare and because they do not lead to perforation without involving the mucosa. Granulomas — tuberculosis and actinomycosis — are also rare in this region and need not be discussed in the absence of more evidence suggesting them. Without more definite evidence concerning the nature of the mucosa in the region of the lesion, one can merely marshal the evidence and then make as good a guess as one can regarding the differentiation of carcinoma and diverticulitis.

The long history of constipation is characteristic of diverticulitis and diverticulosis but does not help us any more than does the demonstration of diverticulums by roentgenograph. In fact, if the patient used daily catharsis for years, it is difficult to be sure he was really constipated. Some change took place in the bowel during the three days before admission, however, for then there were no bowel movements. I assume that the change was inflammatory.

The patient was seventy-eight years old. The ages most frequently encountered in diverticulitis are in the decade between fifty and sixty. When these figures are corrected for the incidence of ages in the general population, however, diverticulitis

enlargement of the cervical veins when he was admitted

DR KING He had everything else, I wish he had had that too

DR MALLORY It is obvious that at one period a malignant tumor was strongly considered. Such a possibility unquestionably underlay the biopsy of the pleura

DR KING I grant you that one has to think of malignant tumor in the differential diagnosis, which I did not mention because of time. But the story is too long in duration, and in addition, the patient had a two-year period when he was perfectly well

#### CLINICAL DIAGNOSES

Lobar pneumonia  
Carcinoma of lung?  
Arteriosclerotic heart disease  
Congestive heart failure  
Pulmonary embolism  
Ventricular fibrillation?

#### DR KING'S DIAGNOSES

Tuberculous constrictive pericarditis  
Tuberculous pleurisy  
Pulmonary tuberculosis  
Pneumococcal pneumonia (Type 3)  
Pulmonary infarcts  
Pulmonary embolus (fatal)  
"Pseudo-cirrhosis of liver"

#### ANATOMICAL DIAGNOSES

Pericarditis, adhesive.  
Pleuritis, fibrous left chest  
Cirrhosis of liver, toxic  
Hydrothorax, right  
Infarcts of lung, multiple, recent  
Pulmonary emboli, multiple  
Bronchopneumonia, organized  
Osteomyelitis, healed right fibula  
Pancreatitis, chronic

#### PATHOLOGICAL DISCUSSION

DR MALLORY Dr King made a number of diagnoses, and I have to list a number of pathological findings. I do not believe I can tie mine together any more satisfactorily than he has.

There was a constrictive pericarditis. The pericardium was densely fibrous, ranging from 3 to 5 mm in thickness, with no calcification at any spot. Microscopically the sections showed almost pure collagen, with only the smallest collections of lymphocytes and nothing to suggest tuberculosis. The left pleural cavity was also completely obliterated by old fibrous adhesions, and at the left base, between the lung and diaphragm, this fibrous tissue was 2 to 3 cm in thickness, being dense and practically cartilaginous in consistence. The right pleural cavity contained a liter of cloudy fluid, probably a terminal accumulation. The lungs showed two distinct types of lesions. There were a

large number of pulmonary infarcts — some quite fresh and others slightly older, none of them were very old, however. There were numerous pulmonary emboli to go with them, including a massive embolus, which apparently caused the sudden death. Also scattered irregularly throughout both lungs, but most marked in the right upper lobe, were areas of old completely organized pneumonia. It is quite clear that these were not infarcts, but it is impossible on the basis of the sections to guess how old the process was. There appeared to be nothing active about it in the terminal period, it might have been months or even years old.

Finally, there was a marked cirrhosis of the liver. This was the coarsely nodular type and, to my eye, did not resemble cardiac cirrhosis, which is so often seen in cases of adhesive pericarditis. It was probably a separate lesion of entirely different etiology. Another incidental finding, probably of no significance, was chronic interstitial pancreatitis of moderate severity.

DR KING And no tuberculosis?

DR MALLORY None anywhere.

DR ALLAN G. BRAILEY Do you think that the bloody pleural fluid was due to infarcts at various times?

DR MALLORY The fluid was found several years before the final entry, if I remember correctly. The old scars in the lung all look like those of organized pneumonia, not of infarcts. I think that is a distinction we can make with reasonable certainty because the scar of a healed infarct is rather characteristic.

DR KING Do these idiopathic processes usually produce as much fever? Have you had cases like this before with persistent temperature?

DR MALLORY I do not dare answer that.

DR BLAND Did the pulmonary infarcts account for the peaks of temperature?

DR KING They might have, I suppose.

DR MALLORY It is rather interesting that, despite the cirrhosis of the liver, the numerous pulmonary infarcts did not produce jaundice in the terminal period, as they commonly do with other types of cardiac disease.

DR BLAND Were the veins examined?

DR MALLORY There were thrombi in the leg veins.

DR KING Was this a pneumococcal pneumonia?

DR MALLORY There was no acute pneumonia. I believe that all the fresh episodes were due to infarction.

#### CASE 32102

#### PRESENTATION OF CASE

A seventy-eight-year-old man entered the hospital complaining of abdominal pain.

During the few months before admission he had occasional bouts of intermittent lower abdominal

the wards essentially paralleled Dr Simeone's reasoning. Diverticulitis was considered the most probable diagnosis, and the sudden episode was interpreted as a perforation. An exploratory laparotomy was performed by Dr J G Scannell. He found a diffuse purulent peritonitis, most marked in the pelvis. The appendix was normal. A mass was found at the rectosigmoid junction that was thought to be inflammatory and secondary to a perforated diverticulum. A transverse colostomy was done, and the patient was put on the usual regime for peritonitis. His general condition steadily deteriorated, and he died on the fifth day after operation.

The post-mortem examination showed a severe diffuse peritonitis that involved all parts of the peritoneal cavity without any localized collection to suggest abscess formation. A mass could be felt at the junction of the sigmoid and rectum that constricted the bowel, reducing the lumen to a diameter

of 2 cm. On opening the bowel a characteristic ulcerative carcinoma was found, with a perforation in the center of the area of ulceration. The perforation was small, and no free fecal material was found in the peritoneal cavity. Although diverticula were present throughout the bowel none showed evidence of inflammation.

The other findings at autopsy were for the most part coincidental. There was massive collapse of the lower lobe of the right lung. The heart showed a hypertensive hypertrophy, and although the coronary arteries were sclerotic and narrowed, there was no evidence of infarction. The gall bladder was large and contained numerous large stones. The major portion of the prostate had been removed, and there was comparatively little regeneration.

Microscopical examination proved the tumor in the bowel to be a well differentiated adenocarcinoma. There were no implantations or metastases.

becomes about as common in occurrence in the older age groups as it is in the fifty-to-sixty group

Diverticulitis is more frequent among males than among females, but this point is of little help in differential diagnosis

Lack of blood in the stools is certainly in favor of diverticulitis, as opposed to carcinoma of the sigmoid. It is true, of course, that some patients with carcinoma do not have blood in the stools and that 10 to 20 per cent of those with diverticulitis do show this sign. Nevertheless, the lack of blood in the stools can be interpreted as strongly in favor of diverticulitis

A mass is felt more frequently with diverticulitis than with carcinoma. No definite statement is made that no mass was palpated, but it can be assumed that none was found. Absence of a mass, however, is not conclusive evidence against diverticulitis

Slight tenderness in both lower quadrants is consistent with diverticulitis. It is equally consistent, although less often elicited, with carcinoma complicated by penetration or perforation. Such a carcinoma, however, should have been demonstrated by obvious mucosal changes in the roentgenogram

The fever and leukocytosis suggest an inflammatory reaction. Although these signs favor diverticulitis, they do not exclude carcinoma, which, as already mentioned, may have an inflammatory reaction about it

Hypoproteinemia and hypochloremia are recorded as isolated occasions. These observations can be assumed to be accurate and are not extraordinary in an old man who has had chronic intestinal obstruction with recent vomiting. The patient may not actually have been as well nourished as he seemed

The roentgenographic finding of diverticula is strongly in favor of diverticulitis as the cause of the patient's symptoms. It does not exclude carcinoma, however, for cancer may coexist with diverticulitis and diverticulosis. The irregularity of the bowel wall is typical of diverticulitis. If we are justified in assuming that no abnormality was detected in the mucosa itself, this is strong evidence against carcinoma. The lack of spasm is against diverticulitis but does not rule it out. The degree to which the lumen was narrowed, if at all, is not stated. If there was little narrowing, the finding would favor diverticulitis

On weighing all the evidence, we find more in favor of diverticulitis than of carcinoma. The reference of pain about the rectum is more consistent with diverticulitis than with uncomplicated carcinoma. The final episode of generalized tenderness and boardlike spasm in the abdomen indicates a generalized peritonitis, which followed shortly after the administration of a barium enema. This is more readily explained on the basis of diverticulitis than on that of carcinoma. It may be

assumed that the manipulation or the pressure developed when unsuccessfully attempting to expel the enema caused perforation of a gangrenous diverticulum. This resulted in a spreading peritonitis. Such occurrences are rare but have been described. The same picture could have been produced by the rupture of an abscess about the area involved in the diverticulitis. This is suggested by the fact that no gas was found beneath the diaphragm by x-ray examination when the patient was examined in the standing position. Absence of demonstrable air beneath the diaphragm, however, does not rule out perforation of the bowel at the site of a diverticulitis. Perforation of a malignant lesion of the colon is not infrequent during proctoscopy or sigmoidoscopy, but I am not aware of such a complication following a barium enema.

The question arises whether perforation may have occurred in the bowel at a site other than that of the lesion itself. Rupture of the large intestine as the result of obstruction in the colon usually occurs in the cecum. Had this taken place in this patient, air beneath the diaphragm would have been expected and there should have been evidence of severer bowel obstruction beforehand than there apparently was

In summary, the patient's long history of constipation, the low abdominal pain and tenderness, the pain in the rectum, the mild fever and leukocytosis, the evidence of incomplete large-bowel obstruction by history and roentgenograph, the x-ray evidence of a partially obstructing lesion in the sigmoid with diverticula nearby and without obvious destruction of the mucosa and the absence of blood in the stools suggest a diagnosis of diverticulitis. The episode that led to emergency surgery was a spreading peritonitis as the result of perforation of an involved diverticulum

#### CLINICAL DIAGNOSES

Peritonitis from perforated viscus  
Hypertension  
Arteriosclerosis

#### DR SIMEONE'S DIAGNOSES

Diverticulitis of colon, with perforation and generalized peritonitis  
Diverticulosis of colon

#### ANATOMICAL DIAGNOSES

Adenocarcinoma of rectosigmoid, with perforation.  
General peritonitis  
Operative wound transverse colostomy  
Cardiac hypertrophy, hypertensive type  
Arteriosclerosis of coronary arteries, moderate  
Arteriosclerosis of aorta, severe  
Pulmonary atelectasis  
Diverticulosis of colon  
Prostatectomy, old, transurethral

#### PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY Clinical discussion on

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## CARDIAC MURMURS

A LETTER published elsewhere in this issue of the *Journal* criticizes the stand taken in a recent paper\* regarding the significance of apical systolic murmurs. Undoubtedly, in the interpretation of heart murmurs the pendulum swung from one extreme to the other thirty years ago, when James Mackenzie urged the medical profession to disregard auscultatory cardiac findings, provided there was an adequate state of the circulatory function. That advice served a useful purpose—it did help win World War I by allowing many able-bodied men with heart murmurs to serve in the British forces. But the interpretation was too literal, and for many years British medicine suffered from its indiscriminate acceptance. One cardiologist states that

as long as ten years after the end of World War I he found cases of clear-cut and clinically significant aortic stenosis on the wards of Thomas Lewis that had been undiagnosed because of the scorn of stethoscopic findings. In other words, the pendulum was still at its extreme. During the last two decades, however, it has become the experience of most cardiologists who went through the earlier period that this casual attitude is not only unscientific but actually dangerous. There are three reasons for this.

In the first place, valvular disease produces a strain on the heart muscle, at times it is slight or moderate, but sometimes it is considerable, even though cardiac function and reserve may, for the moment, be adequate. In almost all cases trouble looms up ahead, and the more careful the patient is to avoid unnecessary strain, the longer is the postponement of trouble. Of course, the development of a crippling neurosis or valetudinarianism should be avoided, but so too should the unnecessary early induction of acute pulmonary edema by a disregard of the considerable strain resulting from a previously symptomless but easily diagnosed aortic stenosis. There is a happy mean in the conduct of such a person's life.

In the second place, a healthy young person with chronic valvular disease is a candidate for recurrent rheumatic fever if exposed to infection by the hemolytic streptococcus, as experience in World War II has so clearly demonstrated. Such a person obviously deserves some protection.

Finally, it is true that one of the most infallible guides to the presence of active rheumatic infection in a doubtful case is the development of a heart murmur *under observation*, especially the controversial apical systolic murmur not explained by anemia or other factors but due to left ventricular dilatation secondary to acute rheumatic myocarditis.

Any moderate or loud apical or aortic systolic murmur in a person *at rest* is best regarded as abnormal unless proved to the contrary. The cause may, of course, be extracardiac, but it should be looked for and diagnosed, whether intracardiac or extracardiac.

No brief should be held for the exaggeration of

\*Wolfson, I. N. Clinical and laboratory studies of 91 workers with apical systolic murmurs. *New Eng J Med* 233:757-761, 1945.

the importance of heart murmurs, in fact their neglect is the lesser of the two evils, but it is possible with care and experience to avoid both extreme points of view and to develop the use of the stethoscope as an extremely valuable medical tool in the diagnosis of heart disease

## SCHOOL-HEALTH POLICIES

School health in its various aspects and the impact of school medical services on health education have received nearly their share of attention in the last decade. It is up to those who are interested in it, however, to see that school health does not fall too far into the category of Mark Twain's New England weather, about which so many have talked and so few have attempted any practical reforms.

The Strayer Report on the Boston Public Schools, published in 1944 in its various volumes, contained recommendations on school lunches and on physical and health education that were considered by a committee of the Boston Health League and, in the main, favorably reported on. The Division of Child Hygiene of the Massachusetts Department of Public Health has developed excellent procedures to be used as guides in the towns and cities of Massachusetts outside Boston, studies have been made jointly by the State Department of Health and the State Department of Education, and many other wise pronouncements the Nation over are available for those who wish to profit by them.

If there is any real reason why the country's schools do not have and do not follow the best and most progressive health policies, it is because of a public that is bent on other forms of whoopee or because of the inertia of municipal politics when applied to academic problems.

The American Academy of Pediatrics interested itself in the problem of school health soon after its organization in 1931 and formed a committee to study the subject. It has published various reports including a statement "Suggested School-Health Policies" produced jointly with the Child Hygiene Section of the American Public Health Association. A revision of this report has been currently made public by the National Conference for Co-operation

in Health Education,\* and the pamphlet includes about all the advice that can be given to anyone interested in establishing school-health policies in any locality.

Particularly important with respect to these modern school-health policies is the necessity of raising school health and health education to the position of dignity and importance that belongs to them. Teachers should be prepared at teachers' colleges to assume their share of the health program, school nursing should be on a career level, the branch of public health that deals with school health and health education should be expected to furnish careers for an adequate number of trained physicians. The school should participate in community health education, and conversely, the community should interest itself in the health policies of its schools. Inside the school, the health council should be a representative body including students and parents, and this council should co-ordinate with the central school-health council and the community health council.

As with so many of life's obstacles, the problem lies not so much in finding a way to follow as in finding the will to follow the way.

## MASSACHUSETTS MEDICAL SOCIETY

### REVIEW LECTURE COURSE

The following is the detailed program of the Review Lecture Course from March 18 to April 15, inclusive.

**March 18 GASTROINTESTINAL DISEASES** Chairmen Sara M. Jordan and Franklin W. White

5:00-5:30 Diagnosis of Cancer of the Digestive Tract  
Franz J. Ingelfinger, assistant professor of medicine, Boston University School of Medicine, gastroenterologist, Massachusetts Memorial Hospitals

5:30-6:00 Functional Diseases of the Digestive Tract  
Sara M. Jordan, chief Department of Gastroenterology, Lahey Clinic, physician, New England Baptist and Deaconess hospitals

6:00-6:30 Ulcerative Colitis  
Isaac R. Jankelson, assistant professor of medicine, Tufts College Medical School, junior visiting physician, Boston City Hospital

7:30-8:00 Epidemiology of Amebiasis and the Dysenteries  
Vlado A. Getting, Commissioner of Public Health, Commonwealth of Massachusetts

8:00-8:30 Diseases of the Small Intestine  
Katherine S. Andrews, surgeon, New England Hospital for Women and Children

8:30-9:00 Some Proctologic Problems  
E. Parker Hayden, assistant in surgery, Harvard Medical School, assistant surgeon, Massachusetts General Hospital

\*The American Academy of Pediatrics and the American Public Health Association. *Suggested School Health Policies*. Second edition revised 57 pp. 1945.



**March 20 DISEASES OF THE LIVER, GALL BLADDER AND PANCREAS** *Chairmen* Chester M. Jones and Leland S. McKittick

3 00-3 45 **Epidemiology of Hepatitis** Roy F. Feemster, director, Division of Local Health Administration, Massachusetts Department of Public Health

3 45-4 30 **Chronic Hepatic Disorders** Chester M. Jones, clinical professor of medicine, Harvard Medical School, physician, Massachusetts General Hospital

4 30-5 15 **Surgery of the Biliary Tract** Charles G. Mixer, surgeon-in-chief, Beth Israel Hospital

5 45-6 30 **Physiotherapy in the Treatment of Arthritis** Arthur Watkins, chief of physical medicine, Massachusetts General Hospital, associate in medicine, Harvard Medical School

**DISEASES OF THE BONES AND JOINTS** *Chairmen* Frank R. Ober and William A. Rogers

7 30-8 15 **Lame Backs** William A. Rogers, instructor in orthopedic surgery, Harvard Medical School, visiting orthopedic surgeon, Massachusetts General Hospital

8 15-9 00 **Lame Shoulders** Frank R. Ober, John B. and Buckminster Brown, Clinical Professor of Orthopedic

The Journal lacks copies of the December 6, 1945 and January 3, 1946, issues. If any subscribers who do not bind their copies have the above-mentioned issues on hand, the Journal will gladly pay 15 cents for each copy left at or mailed to its office (8 Fenway, Boston 15).

5 15-6 00 **Diagnosis and Treatment of Carcinoma of the Pancreas** Richard B. Cattell, surgeon, Lahey Clinic, surgeon, New England Deaconess and Baptist hospitals

**March 25 SURGERY** *Chairmen* Edward D. Churchill and John W. Spellman

5 00-5 30 **Progress Report** F. D. Moore, instructor in surgery, Harvard Medical School, assistant in surgery, Massachusetts General Hospital

5 30-6 00 **Military Surgery** E. D. Churchill, John Homans, Professor of Surgery, Harvard Medical School, chief of West Surgical Service, Massachusetts General Hospital

6 00-6 30 **Shock and Resuscitation** J. E. Dunphy, associate in surgery, Harvard Medical School, senior associate in surgery, Peter Bent Brigham Hospital, visiting surgeon, St. Elizabeth's Hospital

7 30-8 15 **Choice of the Anesthetic Agent** Morris J. Nicholson, anesthesiologist, Lahey Clinic and New England Baptist and Deaconess hospitals

8 15-9 00 **Head Injury** Donald Munro, associate professor of neurosurgery, Boston University School of Medicine, assistant professor of neurological surgery, Harvard Medical School, surgeon-in-chief and head of Department of Neurosurgery, Boston City Hospital

**March 27. SURGERY** *Chairmen* Edward D. Churchill and John W. Spellman

3 00-3 45 **Thermal Burns** Charles C. Lund, assistant professor of surgery, Harvard Medical School, visiting surgeon, Boston City Hospital

3 45-4 30 **Phlebitis, Thrombosis and Embolism** Claude E. Welch, assistant in surgery, Harvard Medical School, assistant visiting surgeon, Massachusetts General Hospital

**ARTHRITIS** *Chairmen* Marian W. Ropes and Howard K. Thompson

4 30-5 15 **Problems in the Treatment of Various Types of Chronic Arthritis** Nathan Sidel, chief of Arthritis Clinic, Beth Israel Hospital, assistant visiting physician, Boston City Hospital, assistant professor of medicine, Tufts College Medical School

5 15-6 00 **Newer Concepts in the Management of Rheumatoid Arthritis With Special Reference to Gold Salts** Theodore Bayles, visiting physician, Robert Breck Brigham Hospital, junior associate in medicine, Peter Bent Brigham Hospital

**April 1 ARTHRITIS** *Chairmen* Marian W. Ropes and Howard K. Thompson

5 00-5 45 **Orthopedic Care of the Chronic Arthritic** John Kuhns, instructor in orthopedic surgery, Harvard Medical School, visiting orthopedic surgeon, Robert Breck Brigham and Infants' hospitals

Surgery, Harvard Medical School, orthopedic surgeon, Peter Bent Brigham Hospital, chief of Orthopedic Department, Children's Hospital

**April 3 FRACTURES** *Chairmen* Frank R. Ober and William A. Rogers

3 00-3 45 **Colles Fracture** Henry C. Marble, assistant in surgery, Harvard Medical School, visiting surgeon, Massachusetts General Hospital, surgeon-in-chief, Chelsea Memorial Hospital

3 45-4 30 **Fractures of the Elbow** Carroll B. Larson, assistant in orthopedic surgery, Massachusetts General Hospital, assistant in surgery, Harvard Medical School

**NEUROSURGERY OF CHILDHOOD** *Chairmen* Franc D. Ingraham and James B. Campbell

4 30-6 00 **Congenital Anomalies, Injuries, Infections, Intracranial and Intraspinal Tumors, Jacksonian Epilepsy, and Lead Encephalitis** Franc D. Ingraham, surgeon-in-chief, Children's Hospital, assistant professor of surgery, Harvard Medical School, James B. Campbell, junior attending surgeon in neurosurgery, Children's Hospital, assistant in surgery, Harvard Medical School

**April 8 KIDNEY AND GENITOURINARY DISEASES** *Chairmen* Laurence B. Ellis and James P. O'Hare

5 00-6 30 **Glomerular Nephritis and Nephrosis** Progress in etiology, pathology, physiology and clinical management. Stanley E. Bradley, instructor in medicine, Boston University School of Medicine, assistant physician, Evans Memorial, Massachusetts Memorial Hospitals, W. Richard Ohler, assistant professor of medicine, Harvard Medical School, chief, Second Medical Service, Boston City Hospital

7 30-8 15 **Urinary-Tract Infections** E. Granville Crabtree, urologist, New England Baptist, Newton and Beth Israel hospitals

8 15-9 00 **The Female Bladder** Samuel N. Vose, professor of genitourinary surgery, Boston University School of Medicine, urologist, Massachusetts Memorial Hospitals

**April 10 PEDIATRICS** *Chairmen* James M. Baty and Joseph Garland

3 00-3 45 **Care and Feeding of Newborn** Stewart H. Clifford, pediatrician, Boston Lying-in Hospital, assistant visiting physician, Children's Hospital

3 45-4 30 **Surgical Procedures in Early Months of Life** Robert Gross, assistant professor of surgery, Harvard Medical School

4 30-5 15 **Immunization Procedures** Allan M. Butler, assistant professor of pediatrics, Harvard Medical School, chief, Children's Medical Department, Massachusetts General Hospital

5 15-6 00 Rheumatic Fever T Duckett Jones director of research, House of the Good Samaritan

April 15 DERMATOLOGY Chairmen John G Downing and C Guy Lane

5 00-6 30 Symposium on Dermatitis, Eczema and Allergy John G Downing professor of dermatology and syphilology, Tufts College Medical School, professor of dermatology, Boston University School of Medicine, dermatologist-in-chief, Massachusetts Memorial, Boston City and St Elizabeth's hospitals C Guy Lane clinical professor of dermatology, Harvard Medical School, chief, Dermatologic Department, Massachusetts General Hospital Francis M Rackemann lecturer in medicine Harvard Medical School, physician, Massachusetts General Hospital John Fromer director, Department of Allergy and Dermatology, Lahey Clinic

7 30-7 50 Treatment and Diagnosis of Cutaneous Disturbances of Nutritional Origin and Endocrine Dysfunction. G Marshall Crawford instructor of dermatology Harvard Medical School, assistant dermatologist, Dermatologic Department, Massachusetts General Hospital

7 15-8 15 Advances in the Treatment of Pyogenic Infections, Psoriasis and Allied Diseases Bernard Appel associate professor of dermatology, Tufts College Medical School, assistant dermatologist, Boston City Hospital

8 15-8 35 Management of Fungous and Parasitic Infections of the Skin Jacob H Swartz assistant professor of dermatology Harvard Medical School, dermatologist, Dermatologic Department, Massachusetts General Hospital

8 35-9 00 Hypertrophies, Atrophies, and Neoplasms of the Skin Francis M Thurmon assistant professor of dermatology, Tufts College Medical School, physician-in-chief, Clinic of Dermatology and Syphilology, Boston Dispensary

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recent requirements a fraud and a deceit that would subject the offender to disciplinary action

The court found that the delegation by the Legislature to the Regents of the authority to make such rules was proper and that, in the absence of action on the subject by the Legislature, the Regents could make the rule in question — (*Buhl v University of State of New York*, 52 N Y S [2d] 511, Dec 29, 1944)

## CORRESPONDENCE

### CARDIAC MURMURS

To the Editor In view of the enormous amount of unnecessary invalidism and psychic trauma caused by physicians who are unable to evaluate systolic murmurs, it seems unfortunate that Wolfson's communication, "Clinical and Laboratory Studies of Ninety-One Workers with Apical Systolic Murmurs," which appeared in the December 20, 1945, issue of the *Journal*, did not elicit at least a modifying editorial comment.

The author states, "A murmur was considered to be associated with a cardiovascular abnormality when the patient had a history of rheumatic fever [a doubtfully valid assumption], hypertension, roentgenologic evidence of cardiac enlargement, an abnormal electrocardiogram, or other disease that might be expected to produce a murmur [again, a doubtful assumption unless one considers the hemic murmur of anemia to be evidence of a cardiovascular abnormality]"

The author also states "In the youngest age group, below twenty-five, a history of rheumatic fever was obtainable in more than half the cases. From this it may be concluded that an apical systolic murmur in a young patient is likely to be associated with rheumatic fever."

On going back to the author's criteria for a past history of rheumatic fever, however, one finds the following statement "Careful inquiries were made for a past history of rheumatic infection, and this was said to be positive only when it included at least one of the following an illness characterized by swollen, painful, tender joints, an illness of several weeks' duration, diagnosed at the time by the attending physician as rheumatic fever, *prolonged bed rest recommended by a physician because of the discovery of a heart murmur* [italics mine], and St. Vitus's dance." It seems most unfortunate that the author accepts "prolonged bed rest recommended by a physician because of the discovery of a heart murmur" as evidence of rheumatic infection. I believe that this assumption is entirely unjustified and, as often as not, represents an incorrect diagnosis on the part of the attending physician.

Judging from personal experience in a small outpatient cardiac clinic (Cambridge Hospital) on the medical ward service of a large city hospital (Boston City Hospital) and in the internists' department at an induction center (First Service Command), I believe that the finding of an apical systolic murmur as the sole sign of a cardiac disorder in a person under twenty-five without hypertension, hyperthyroidism, tachycardia, fever, anemia or a clear-cut history of rheumatic fever is better ignored than studied.

This I believe, is still true even in the presence of organic heart disease. An apical systolic murmur in the absence of cardiac enlargement (by x-ray) or diminished exercise tolerance is no contraindication to normal physical activity, including strenuous sports, and should never be the reason for putting a person to bed for weeks or months.

The incidence of cardiac neuroses and unnecessary cardiac invalidism in young people with systolic murmurs is a most unfavorable commentary on the practicing physicians in this country. The stethoscope is a double-edged sword, and I still agree with MacKenzie that the physician would do well to throw away his stethoscope while evaluating cardiac murmurs.

DUDLEY MERRILL, M.D.

50 Brattle Street  
Cambridge, Massachusetts

## MEDICOLEGAL ABSTRACT

**Regulation of Practice by Government Qualifications to Practice** A man who had taken out life insurance from the defendant company died. The plaintiff was his beneficiary. The policy contained a clause which provided that, if the insured had received medical or surgical treatment within two years prior to his application for insurance and had not disclosed this fact on the application, the policy would be voidable. The deceased did receive treatments from a chiropractor within the period and did not disclose this fact.

The beneficiary brought suit to recover the proceeds of the policy, which the company refused to pay on the grounds that the treatment by the chiropractor was undisclosed medical or surgical treatment rendering the policy voidable. The trial court refused to direct a verdict for the defendant, and the defendant appealed. In reversing the judgment, the Supreme Court of New Jersey said that the Legislature had regulated the practice of chiropractic under "an act to regulate the practice of medicine and surgery" and that it was within the power of the Legislature to so classify it — (*Kahn v Metropolitan Life Insurance Company*, 41 Atl [2d] 329, March 1, 1945, New Jersey).

In New York, however, possession of a mere license to practice podiatry or chiropody, without more, does not confer on the licensee the right to call himself "doctor."

Originally the educational requirements to practice podiatry and chiropody were one year of college and three years of professional training. Subsequently they were increased, and graduates were admitted to the degree of doctor of podiatry or chiropody. This placed those who were licensed under the original requirements at a disadvantage, and they sought to call themselves "doctor" too. They therefore brought an action seeking to have rescinded a rule promulgated by the Regents of the State University declaring the use of the title "doctor" by those who had not fulfilled the more

## NOTICES

## ANNOUNCEMENTS

Dr William W Babson announces his return to the practice of surgery at 79 Prospect Street, Gloucester

Dr James R Corkery, having returned from military service, has resumed practice at 6 Hancock Street, Everett

Dr Sidney Derow, having been released from active duty with the United States Navy, has resumed his practice at 925 Centre Street, Newton Centre

Dr Clifford C Franseen announces his return from military service and the reopening of his offices at 1180 Beacon Street, Brookline, for the practice of surgery

Dr Irvin G Gahm announces his return from military service and resumption of practice at 414 Walnut Street, Newtonville

Dr Stuart N Gardner, having returned from service with the United States Navy, announces the reopening of his office at 24 Chestnut Street, Salem, for the practice of internal medicine

Dr A Gordon Gauld announces the reopening of his office for the practice of obstetrics and gynecology at 330 Dartmouth Street, Boston

Dr Richard J Gorman, having returned from service with the United States Navy, announces the opening of his office at 628 Centre Street, Jamaica Plain, for the general practice of medicine

Dr Lyman H Hoyt, having returned from service in the Medical Corps of the United States Navy, has resumed his practice at 51 Bay State Road, Boston

Dr Samuel W Joel announces his return from military service and the reopening of his office for the practice of psychiatry and neurology at 510 Commonwealth Avenue, Boston

Dr William E Ladd announces the removal of his office from the Children's Hospital to 330 Dartmouth Street, Boston

Dr William N Lanigan, recently released from military service, announces the reopening of his office at 187 Main Street, Medford, for the practice of orthopedic surgery

Dr Charles C Lund announces the removal of his office from 319 Longwood Avenue to 20 Gloucester Street, Boston

Dr Charles J McCarthy has been released from military service and has resumed the practice of medicine at 466 Medford Street, Somerville

Dr John D Shinberg, having returned from the armed services, announces the reopening of his office at 54 Merrimack Street, Haverhill

## MEDICAL LIBRARY ASSOCIATION

The Medical Library Association will hold its postwar convention at the Yale Medical Library, New Haven, Connecticut, on March 25, 26 and 27. The program will include papers on the history of medicine in Connecticut by Drs Herbert Thoms and Harold S Burr and on the libraries of Yale University by Mr J T Babb, Dr John F Fulton and others. Dr Sanford V Larkey will speak on his experiences as medical historian of the European Theater. Miss Ethel Wigmore, of the National Institute for Medical Research, will discuss British and Continental medical libraries. There will also be reports on the organization of the Army Medical Library by members of its staff and general discussions on interlibrary and international co-operation. The training necessary for medical librarianship is the subject chosen for the presidential address by Miss Mary Louise Marshall. The speaker at the annual banquet will be Professor C-E A Winslow. Headquarters will be at the Hotel Taft. Further details may be obtained from the secretary—Miss Frida Plieffe, 2000 Medical Arts Building, Minneapolis, Minnesota.

## SOCIETY MEETINGS AND CONFERENCES

## CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MARCH 14

## FRIDAY MARCH 15

\*9:00-10:00 a.m. Clinicopathological Conference Drs Chester S Keefe and H E MacMahon Joseph H Pratt Diagnostic Hospital

\*10:00 a.m.-12:00 m Medical Staff Rounds Peter Bent Brigham Hospital

10:50 a.m. Ultraviolet Radiation Therapy in Diseases of the Skin Dr Edward LaFreniere (Postgraduate Clinic in Dermatology and Syphilology) Amphitheater, Dowling Building Boston City Hospital

## MONDAY MARCH 18

\*12:00 m-1:00 p.m. Clinicopathological Conference Peter Bent Brigham Hospital

## TUESDAY, MARCH 19

\*12:15-1:15 p.m. Clinicorontgenological Conference Peter Bent Brigham Hospital

## WEDNESDAY MARCH 20

\*9:00-10:00 a.m. Diagnostic Errors in the Pratt Hospital Dr C B Popplestone Joseph H Pratt Diagnostic Hospital

\*10:30-11:30 a.m. Medical Clinic Isolation Building Amphitheater Children's Hospital

\*12:00 m. Clinicopathological Conference (Children's Hospital) Amphitheater, Peter Bent Brigham Hospital

\*2:30-4:00 p.m. Combined Clinic by the Medical Surgical and Orthopedic Services Amphitheater Children's Hospital

\*Open to the medical profession

JANUARY 7-APRIL 22 1946 Metropolitan State Hospital Eleventh postgraduate seminar in neurology and psychiatry Page 314, issue of September 6

FEBRUARY 4-MARCH 29 Health Education Institute Page 746, issue of December 13

MARCH 11 Massachusetts Hospital Association Page 240 issue of February 14

MARCH 12 Greater Boston Medical Society Page 312 issue of February 28

MARCH 12 Harvard Medical Society Amphitheater, Peter Bent Brigham Hospital 8:00 p.m.

MARCH 14 Buritis at the Shoulder Joint Diagnosis and treatment. Drs Francis C Hall and Robert B Osgood Pentucket Association of Physicians 8:30 p.m. Haverhill

MARCH 15-SEPTEMBER 15 Boston University Course for Discharged Medical Officers Page 240 issue of February 14

MARCH 25-27 Medical Library Association Notice above.

APRIL 1-JUNE 1 Intensive Course in Ophthalmology Page 240 issue of February 14

APRIL 4 Hermann M Biggs Memorial Lecture Page 206 issue of February 7

MAY 13-17 American College of Physicians Page 798, issue of December 20

JUNE 20-22 American Association for the Study of Gout Page 317 issue of February 28

## DISTRICT MEDICAL SOCIETY

## WORCESTER

MARCH 13 Worcester Memorial Hospital

APRIL 10 Hahnemann Hospital

MAY 8 Annual meeting

# The New England Journal of Medicine

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Number 11

## TRAUMA OF THE LOWER URINARY TRACT\*

### A Roentgenologic Study

H STEPHEN WEENS M.D. † J HAROLD NEWMAN M.D. ‡ AND THOMAS J FLORENCE M.D. §

ATLANTA, GEORGIA

**I**NJURIES of the bladder and posterior urethra constitute surgical emergencies. Appropriate therapy instituted early, usually gives gratifying results, but delay in treatment causes a sharp increase in the morbidity and mortality. It is therefore important that there be available safe, simple and reliable diagnostic procedures.

The clinical history and physical examination may provide sufficient information to establish a diagnosis, but oftener they serve only to focus attention on the lower urinary tract without permitting a definite conclusion concerning the exact site and extent of the injury. The urinalysis may even be deceptive. Intraperitoneal rupture of the bladder can exist in the presence of grossly clear urine<sup>1</sup> and conversely, hematuria may occur in the absence of significant injury to the urinary tract.

Diagnostic procedures that utilize a catheter introduce a new element of trauma in urethral injuries. Urinary flow after introduction of a catheter does not exclude vesical rupture, since urine may be drained from the peritoneal cavity. For the same reason, recovery of measured quantities of fluid introduced into the bladder through a catheter does not permit exclusion of vesical injuries.

The value of cystoscopy in trauma of the lower urinary tract is the subject of much controversy. It constitutes a comparatively major procedure that may aggravate the injury and often fails to establish a diagnosis. The demonstration of injury to the urinary bladder by the intravesical injection of air has certain disadvantages. In the presence of pelvic trauma it is usually difficult to obtain the necessary roentgenograms with the patient in the upright and recumbent positions. Furthermore, the danger of air embolism cannot be lightly dismissed.<sup>2</sup>

Most recent authors<sup>3-5</sup> agree that urethrography

and cystography with a radio-opaque medium represent the most satisfactory diagnostic procedures available. With these methods one should be able to demonstrate any injury that interrupts the continuity of the urethra or bladder. This may be accomplished with a minimum of manipulation, pain and trauma. Although much emphasis has been placed in the recent literature on the value of these diagnostic procedures, little attention has been given to their correct interpretation. Culp<sup>4</sup> in an analysis of a large series of cases of ruptured urethra and bladder, states that retrograde cystograms showed extravasation in every case in which they were employed and that the chief difficulty encountered was failure to interpret accurately the extent of extravasation. Lewis<sup>5</sup> cites a case of intraperitoneal rupture of the bladder in which cystography was performed but because of failure of interpretation the diagnosis was not made.

For these reasons it was thought worth while to report 7 cases of trauma of the lower urinary tract with emphasis on the salient roentgenologic features.

**CASE 1.** L. L. H. (A-37673) a 24-year-old woman was admitted 48 hours after having been injured in an automobile accident. She had not voided or had a desire to do so since the time of the injury. Shortly before admission a local physician had catheterized the patient and obtained 2000 cc of bloody urine. On examination the patient was markedly distended and had the classic signs of generalized peritonitis. An intravenous pyelogram demonstrated normal urinary passages, including a normal bladder (Fig. 1). A Foley catheter was introduced, and 200 cc of bloody urine was obtained. Since a bladder injury was still suspected, a retrograde cystogram was made. It revealed extensive intraperitoneal extravasation (Fig. 2). Therapy consisted of drainage of the bladder with a Foley catheter, chemotherapy, parenteral nutrition and intestinal decompression with a Miller-Abbott tube. The patient made an uneventful recovery and was discharged on the 19th hospital day.

**Comment.** This case illustrates the fact that recovery of large volumes of urine after catheterization does not exclude vesical injury. Apparently the large amount of urine obtained by catheterization was drained chiefly from the peritoneal cavity.

**CASE 2.** T. J., (A-85633), a 45-year-old man, was admitted in an intoxicated, disoriented condition shortly after an automobile accident. X-ray examination showed dislocation of the left sacroiliac joint and fractures of several ribs. The

\*From the Department of Roentgenology and the Department of Urology, Grady Memorial Hospital, Emory University School of Medicine.

†Roentgenologist, Grady Memorial Hospital.

‡Formerly resident in urology, Grady Memorial Hospital.

§Resident in urology, Grady Memorial Hospital.



left humerus and both pubic bones. The patient was unable to void, and 100 cc of grossly bloody urine was obtained by catheterization. Two hundred and fifty cubic centimeters of sterile water was injected into the bladder, and the same amount was recovered by aspiration. Since signs of peritonitis developed, an intravenous pyelogram was performed. This revealed no traumatic changes in the upper urinary tract. The urinary bladder was not visualized. A subsequent retrograde cystogram disclosed intraperitoneal extravasation (Fig 3). On exploratory laparotomy a stellate laceration

to No 30 Fr with graduated curved Van Buren sounds. A No 28 Fr Stern-McCarthy electrotome was introduced, and inspection preliminary to prostatic resection was performed. The field was obscured by blood, and a diminished quantity of the irrigating fluid seemed to return. The bladder could not be sufficiently distended to visualize its interior satisfactorily. As the anesthetic reached the level of the umbilicus, the patient began to complain of epigastric pain. Rupture of the bladder was suspected, and a cystogram was performed. It revealed intraperitoneal extravasation (Fig 4).



FIGURE 1 Case 1

*This is a normal excretory cystogram in a patient with intraperitoneal rupture of the urinary bladder*

of the bladder dome 2 cm. in width was found and repaired. The peritoneum was closed, and a cystostomy was performed. The patient died of peritonitis on the 4th postoperative day.

*Comment.* This case demonstrates that injection and recovery of measured quantities of fluid is not a reliable procedure in the detection of rupture of the bladder.

**CASE 3** G W M (A-110617), a 69-year-old man was admitted with acute urinary retention resulting from fibrous contracture of the vesical neck, which was relieved by inserting a small urethral catheter. He was given a spinal anesthetic on the 6th hospital day, and the urethra was dilated

Exploratory laparotomy disclosed a small rent in the bladder dome. This was sutured, and cystostomy was performed. Recovery was uneventful.

*Comment.* Even though cystoscopy was facilitated by spinal anesthesia in this case, it was impossible to visualize the rent in the bladder.

**CASE 4** W J (A-110131) a 23-year-old woman, was admitted shortly after an automobile accident in which she sustained fractures of the left femur, the right clavicle and both pubic bones. A specimen of urine obtained by catheterization was grossly bloody. After insertion of a Foley

catheter a cystogram was made. This disclosed extensive diffusion of the contrast medium into the pelvic tissues (Fig 5). Exploratory laparotomy revealed no injury of any intraperitoneal structure. After closure of the peritoneum the retroperitoneal space was investigated and laceration of the bladder wall 3 cm. in length was found. Suprapubic cystos-

CASE 5 V V (A-113043), a 40-year-old woman, was admitted after an automobile accident, she was suffering from dyspnea and complaining of pain on respiration. Roentgenologic examination disclosed multiple rib fractures and emphysema of the chest wall. There were bilateral fractures of the pubic rami and a linear fracture of the sacrum. Equivo-

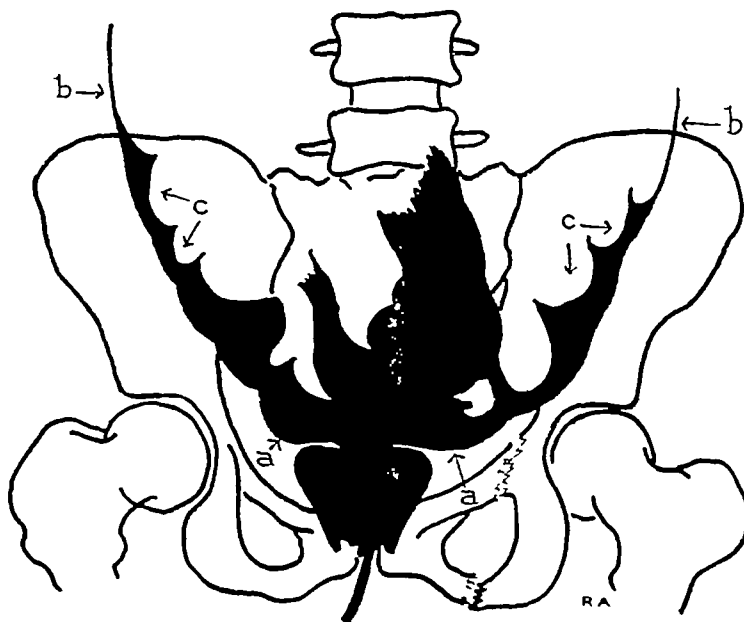
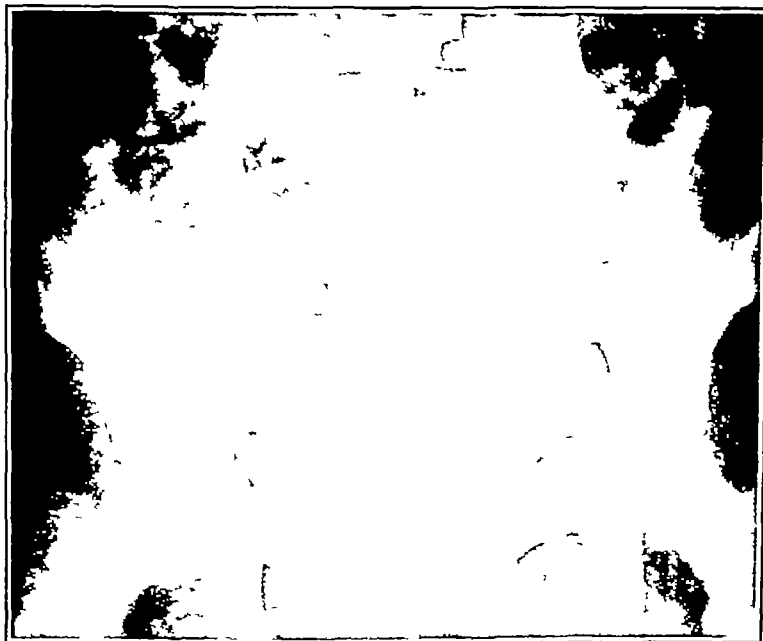


FIGURE 2 Case 1

*This is a retrograde cystogram showing extensive intraperitoneal extravasation. Note the accumulation of contrast medium in dependent portions of the peritoneal cavity (a) and the paracolic recesses (b), as well as the scalloped filling defects of the contrast medium produced by the intestinal loops (c).*

tomy and drainage of the retroperitoneal space resulted in an uneventful recovery.

**Comment.** The extravasated contrast medium in this case assumed a pattern believed to be characteristic of extraperitoneal rupture of the bladder.

cal signs of peritoneal irritation were present in the right lower quadrant of the abdomen.

Because the urine was grossly bloody, a cystogram was performed. It revealed extensive extraperitoneal extravasation of the contrast medium (Fig 6). On laparotomy no

left humerus and both pubic bones. The patient was unable to void, and 100 cc of grossly bloody urine was obtained by catheterization. Two hundred and fifty cubic centimeters of sterile water was injected into the bladder, and the same amount was recovered by aspiration. Since signs of peritonitis developed, an intravenous pyelogram was performed. This revealed no traumatic changes in the upper urinary tract. The urinary bladder was not visualized. A subsequent retrograde cystogram disclosed intraperitoneal extravasation (Fig 3). On exploratory laparotomy a stellate laceration

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*Comment.* Even though cystoscopy was facilitated by spinal anesthesia in this case it was impossible to visualize the rent in the bladder.

**CASE 4** W J (A-110131) a 23-year-old woman, was admitted shortly after an automobile accident in which she sustained fractures of the left femur, the right clavicle and both pubic bones. A specimen of urine obtained by catheterization was grossly bloody. After insertion of a Foley

catheter a cystogram was made. This disclosed extensive diffusion of the contrast medium into the pelvic tissues (Fig 5). Exploratory laparotomy revealed no injury of any intraperitoneal structure. After closure of the peritoneum the retropubic space was investigated and laceration of the bladder wall 3 cm in length was found. Suprapubic cystos-

CASE 5 V V (A-115043), a 40-year-old woman, was admitted after an automobile accident, she was suffering from dyspnea and complaining of pain on respiration. Roentgenologic examination disclosed multiple rib fractures and emphysema of the chest wall. There were bilateral fractures of the pubic rami and a linear fracture of the sacrum. Equivo-

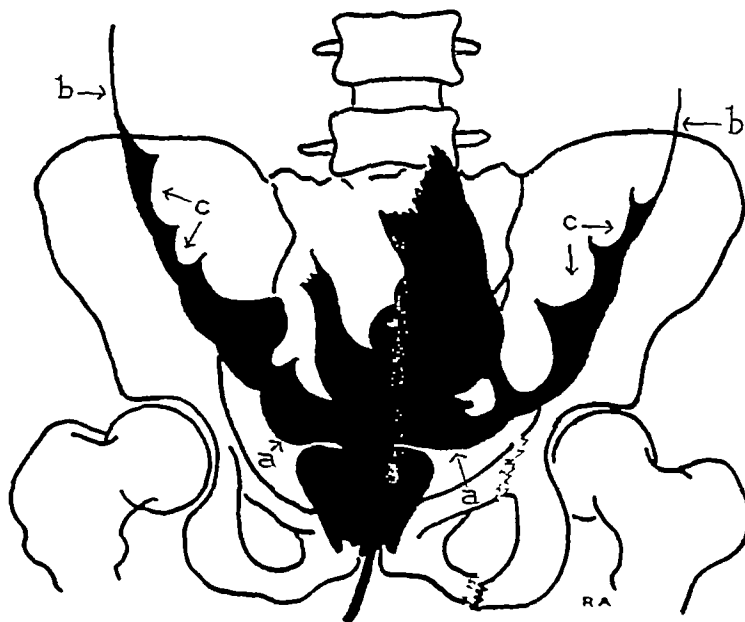


FIGURE 2 Case 1

*This is a retrograde cystogram showing extensive intraperitoneal extravasation. Note the accumulation of contrast medium in dependent portions of the peritoneal cavity (a) and the paracolic recesses (b), as well as the scalloped filling defects of the contrast medium produced by the intestinal loops (c).*

tomy and drainage of the retropubic space resulted in an uneventful recovery.

*Comment:* The extravasated contrast medium in this case assumed a pattern believed to be characteristic of extraperitoneal rupture of the bladder.

cal signs of peritoneal irritation were present in the right lower quadrant of the abdomen.

Because the urine was grossly bloody, a cystogram was performed. It revealed extensive extraperitoneal extravasation of the contrast medium (Fig 6). On laparotomy no

left humerus and both pubic bones. The patient was unable to void, and 100 cc of grossly bloody urine was obtained by catheterization. Two hundred and fifty cubic centimeters of sterile water was injected into the bladder, and the same amount was recovered by aspiration. Since signs of peritonitis developed, an intravenous pyelogram was performed. This revealed no traumatic changes in the upper urinary tract. The urinary bladder was not visualized. A subsequent retrograde cystogram disclosed intraperitoneal extravasation (Fig 3). On exploratory laparotomy a stellate laceration

to No. 30 I r with graduated curved Van Buren sounds. A No. 28 Fr Stern-McCarthy electrotome was introduced and inspection preliminary to prostatic resection was performed. The field was obscured by blood, and a diminished quantity of the irrigating fluid seemed to return. The bladder could not be sufficiently distended to visualize its interior satisfactorily. As the anesthetic reached the level of the umbilicus, the patient began to complain of epigastric pain. Rupture of the bladder was suspected, and a cystogram was performed. It revealed intraperitoneal extravasation (Fig 4).



FIGURE 1 Case 1

*This is a normal excretory cystogram in a patient with intraperitoneal rupture of the urinary bladder.*

of the bladder dome 2 cm in width was found and repaired. The peritoneum was closed, and a cystostomy was performed. The patient died of peritonitis on the 4th postoperative day.

**Comment.** This case demonstrates that injection and recovery of measured quantities of fluid is not a reliable procedure in the detection of rupture of the bladder.

**CASE 3.** G W M (A-110617), a 69-year-old man, was admitted with acute urinary retention resulting from fibrous contracture of the vesical neck, which was relieved by inserting a small urethral catheter. He was given a spinal anesthetic on the 6th hospital day, and the urethra was dilated

Exploratory laparotomy disclosed a small rent in the bladder dome. This was sutured, and cystostomy was performed. Recovery was uneventful.

**Comment.** Even though cystoscopy was facilitated by spinal anesthesia in this case, it was impossible to visualize the rent in the bladder.

**CASE 4.** W J (A-110131), a 25-year-old woman, was admitted shortly after an automobile accident in which she sustained fractures of the left femur, the right clavicle and both pubic bones. A specimen of urine obtained by catheterization was grossly bloody. After insertion of a Foley

intrapertoneal injury was present. After closure of the peritoneum a laceration of the anterior bladder wall 5 cm in length was found. Treatment consisted of suprapubic cystos-

tomized with fractures of both pubic bones and the left wing of the sacrum, sustained in an automobile accident. Shortly after admission he voided 500 cc of bloody urine with con-

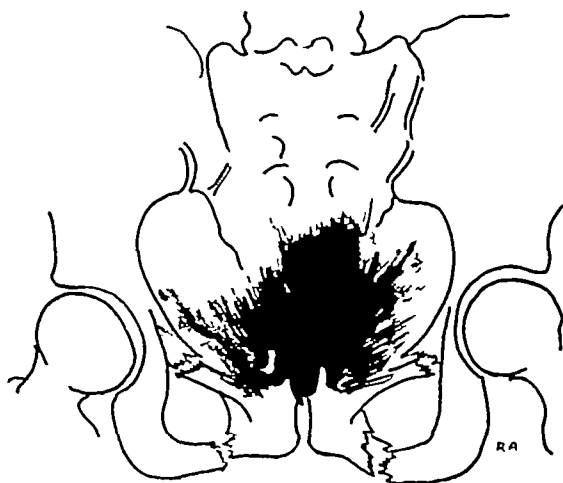


FIGURE 5 Case 4

*This retrograde cystogram shows the findings in a case of extraperitoneal rupture of the urinary bladder. There is extensive diffusion of the contrast medium into the pelvic tissues producing a sunburst-like appearance. Note the absence of filling defects caused by the intestinal loops. There is no pooling of the contrast medium in the dependent portions of the peritoneal cavity, such as occurs in intraperitoneal rupture.*

tomy with drainage of the space of Retzius. The patient made a satisfactory recovery.

*Comment:* In this case laparotomy confirmed the roent-

considerable pain. Examination revealed no tumefaction in the hypogastrium, perineum or rectum. Retrograde urethro-

cystograms showed extravasation in the region of the bladder.

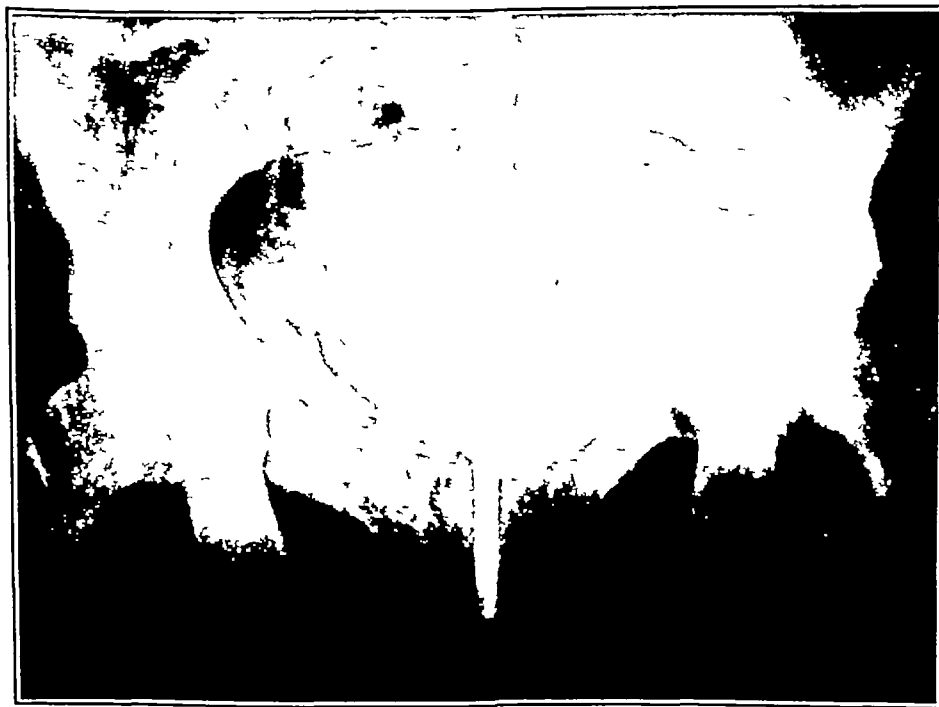


FIGURE 6 Case 5

*This is a retrograde cystogram in another case of extraperitoneal extravasation. The contrast medium has penetrated into the tissues of the pelvic floor and pre-sacral space. Note the pyriform contour and displacement of the urinary bladder.*

roentgenologic diagnosis of an exclusively extraperitoneal bladder injury.

CASE 6 J. W. (A-111627), a 38-year-old man, was ad-

mitted with fractures of both pubic bones and the left wing of the sacrum, sustained in an automobile accident. Shortly after admission he voided 500 cc of bloody urine with con-

neck (Fig. 7). The bladder had a smooth, elongated pyriform contour. The initial therapy consisted only of drainage with a Foley catheter and chemotherapy. A septic course ensued.

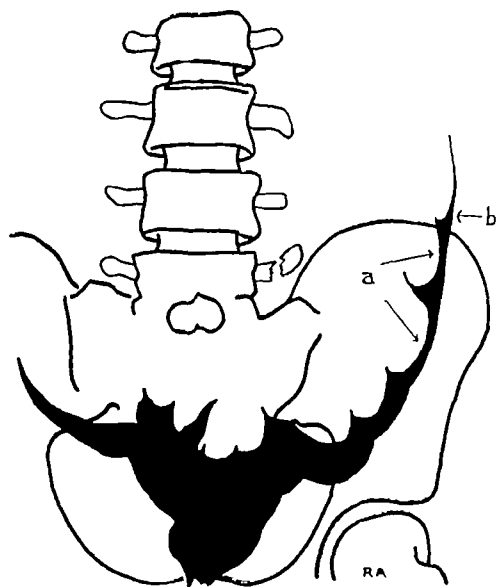


FIGURE 3 Case 2

*This retrograde cystogram shows intraperitoneal extravasation, with accumulation of the contrast medium between the intestinal loops (a) Note the contrast medium in the paracolic recess (b)*



FIGURE 4 Case 3

*This is another retrograde cystogram showing intraperitoneal extravasation. Note the characteristic filling defects in the extravasated contrast medium produced by the intestinal loops*

frequently distended with gas cast characteristic filling defects in the extravasated contrast medium. These defects are round or cylindrical and are recognized without difficulty (Figs 2, 3 and 4). A second and most significant roentgenologic sign is produced by the accumulation of contrast medium as a band-like or linear density along the peritoneal reflection of the flanks (paracolic recesses) (Figs 2 and

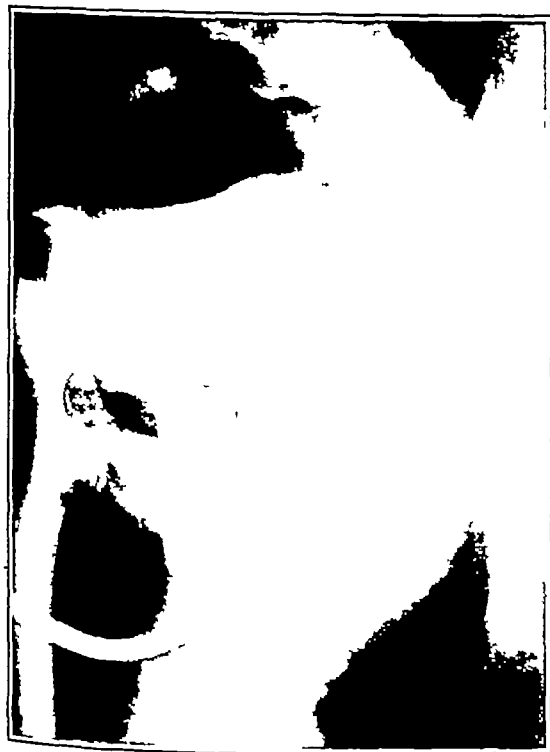


FIGURE 8 Case 7

*This is a normal retrograde cystogram after the injection of contrast medium through the catheter*

3) The radio-opaque medium, even in a low concentration or in small amounts, is easily visible because of the sharp contrast furnished by the subperitoneal layer of fat. Likewise, the haustral markings of the colon and loops of small intestine may produce a scalloped impression along the inner aspect of these bands of increased density (Figs 2 and 3). For these reasons, film studies made in cases of suspected intraperitoneal rupture should include the entire abdomen and its walls.

In contrast, posterior urethral and extraperitoneal vesical ruptures are characterized by more or less diffuse penetration of the contrast medium into the tissues of the pelvic floor and prevesical space. In massive extravasations the medium may assume a sunburstlike appearance (Fig 5). Smaller extravasations are represented by streaks and feathery bands extending from the urinary bladder toward the surrounding soft-tissue structures (Figs 6 and 7). The urinary bladder is frequently deformed in extraperitoneal extravasations. It may assume an elongated pear-shaped appearance or may be dislocated in any direction (Fig 7). Such a deformity

should be considered only as a presumptive sign, since similar changes in the configuration of the bladder may be caused by large pelvic hematomas and abscesses.

The combination of intraperitoneal and extraperitoneal rupture of the urinary bladder was not encountered in this small series. The roentgenologic features of both conditions may be expected in such a combination. The signs of intraperitoneal rupture are likely to be predominant, since the peritoneal cavity probably offers less resistance to extravasating fluids than do the paravesical tissue spaces.

It should be emphasized that intravenous pyelography may produce a seemingly satisfactory

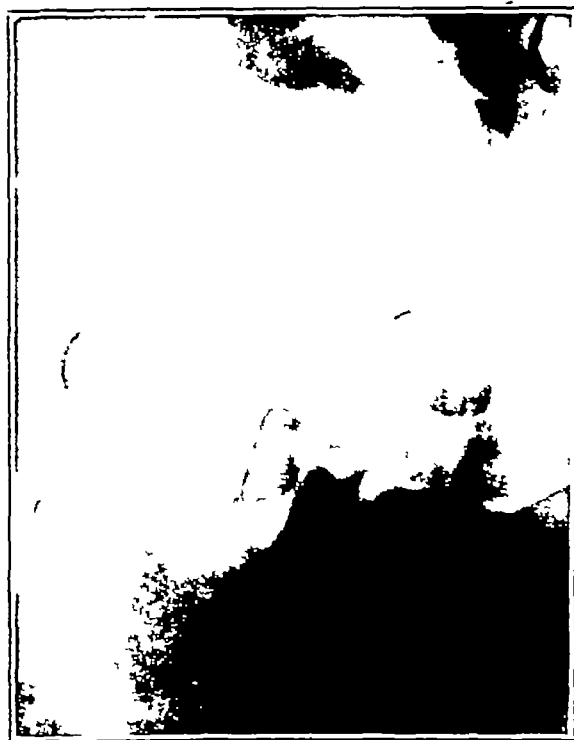


FIGURE 9 Case 7

*This is a retrograde urethrocytogram in the same patient as shown in Figure 8. Note the extensive extravasation in the region of the posterior urethra*

cystogram but is highly unreliable in the diagnosis of trauma of the lower urinary tract. It may fail to demonstrate extravasation because of insufficient density of the medium or because the bladder is not filled under sufficient pressure to produce leakage. This fact is illustrated by Case 1, in which the excretory cystogram showed a well filled bladder with the contrast medium in good concentration (Fig 1) but failed to demonstrate the extravasation that was subsequently discovered by a retrograde cystogram (Fig 2). Suprapubic pressure or straining by the patient may make it possible to demonstrate extravasation in cases in which an adequate excretory urogram has been obtained.

It is also important to note that normal cystograms may be obtained in urethral injuries when a catheter has been passed over the urethral rent into



but responded to suprapubic cystostomy and free drainage of the extravasated area

*Comment* In this case it was impossible to determine from the urethrocytogram whether the injury involved the bladder base or the prostatic urethra. An intraperitoneal rupture, however, could be excluded with certainty

**CASE 7 C D (A-107554)**, a 36-year-old man, was admitted shortly after an automobile accident. X-ray examination disclosed fractures of both pubic bones. Because of difficult urination and gross hematuria, a catheter was intro-

duced into the bladder and a cystogram was made. In females, a catheter is preferable, since it may be introduced with ease and facilitates the injection of the contrast medium. Vaginal palpation with the catheter in place usually permits adequate examination of the urethra.

The volume of contrast medium\* introduced should be individualized. A preliminary roent-

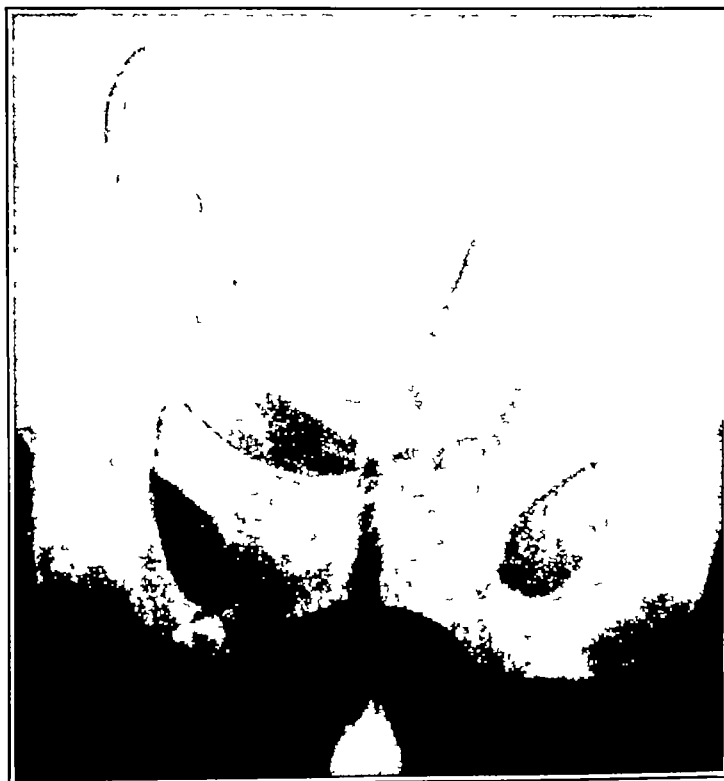


FIGURE 7 Case 6

*This is a retrograde cystogram in a case of extraperitoneal extravasation following trauma of the posterior urethra or bladder neck. Note the elongated pyriform contour of the bladder.*

duced into the bladder and a cystogram was made. The bladder had a normal contour, and no extravasation was demonstrated (Fig 8). The catheter was left in place but accidentally came out after 2 days. At that time retrograde urethrocytograms were obtained, which demonstrated extravasation of the contrast medium in the region of the posterior urethra (Fig 9). Perineal and rectal palpation failed to reveal evidence of extravasation at any time. The catheter was reinserted, and recovery ensued without further treatment.

*Comment* This case illustrates the fact that a cystogram performed after the introduction of a catheter into the bladder may fail to demonstrate an injury of the posterior urethra.

## DISCUSSION

The technic of urethrocytography and the appearance of the normal urethrocytogram have been described by several authors<sup>6, 7</sup> and will not be discussed herein. Various mechanical devices have been advocated for these procedures, and they are undoubtedly of high value. Nevertheless, adequate studies may be obtained without special instruments. An Asepto syringe suffices to introduce the contrast medium. In males, injection of the contrast medium through the urethra permits adequate

visualization of the entire urethra and bladder. In females, a catheter is preferable, since it may be introduced with ease and facilitates the injection of the contrast medium. Vaginal palpation with the catheter in place usually permits adequate examination of the urethra.

The roentgenologic diagnosis of rupture of the bladder and posterior urethra depends on the demonstration of extravasated contrast medium. Although the exact site of leakage is often obscured, it is possible by the pattern and distribution of the contrast medium to distinguish posterior urethral and extraperitoneal vesical injuries from those occurring on the peritoneal surface of the bladder.

In intraperitoneal rupture of the bladder, the opaque medium has a tendency to accumulate and penetrate into the more dependent portions of the pelvic peritoneal cavity when the patient assumes a supine position. The intestinal loops, which are

\*In these studies a 20 per cent solution of Skiodan was used.

episodes of meningococcal meningitis separated by an interval of fourteen months, during which several infections of the upper respiratory tract and two severe attacks of tonsillitis occurred. Some doubt as to the source of the new infection was raised by this author, however, since at the time of his second attack there were several other cases of the disease in the area where the patient lived. Only 1 case in which subacute bacterial endocarditis due to *N meningitidis* may have been the site of origin of a recurrent attack of meningococcal meningitis has been reported in the literature (Lemierre, Laporte, Reilly and Laplane<sup>9</sup>). This patient had two attacks, preceded by bacteremia, one hundred and nine days apart. In the interval, he was apparently completely well. He recovered from the second episode, returned to work on a farm and was in apparent good health until seventeen months later, when he died shortly after having developed a hemiplegia. Post-mortem examination revealed an endocarditis of the aortic valve, with new and old vegetations, and a recent septal infarct of the brain.

The purpose of reporting the case presented below is to describe a true recurrence of meningococcal meningitis in a patient who was in the nephrotic phase of chronic diffuse glomerulonephritis. This patient had two episodes of meningitis and one of lobar pneumonia within a period of sixteen months. The possible relation of the nephrosis to the obviously decreased resistance to bacterial disease is an interesting subject for speculation, since the nephrotic state resulted from a chronic glomerulonephritis and was not of the so-called "lipoid" variety, in which great susceptibility to infection, particularly by a pneumococcus, is the rule.

#### CASE REPORT

C. C., a 22-year-old, unmarried woman, was admitted to the Haynes Memorial Hospital on November 14, 1944, with a diagnosis of meningitis. The family history was irrelevant. In 1941, generalized edema and "cloudy" urine had developed after a sore throat. A diagnosis of diffuse glomerulonephritis was made at that time, and the patient remained under medical observation for the next 3½ years, during which time she had varying degrees of edema, headache and hematuria but no hypertension. On March 26, 1944, she was admitted to the Newton Hospital because of pain in the fingers, nausea, vomiting, malaise, shaking chills, severe pain in the lower back and hips and transient periods of delirium of 24 hours' duration.

The temperature on this admission was 102°F, the pulse 100, the respirations 30, and the blood pressure 132/90. The skin was covered with petechiae, all the deep reflexes were hyperactive, the neck was stiff, and the Kernig and Brudzinski signs were strongly positive. Lumbar puncture revealed the spinal fluid to be under increased pressure and to contain 2400 cells, of a type not stated. The protein and glucose levels were 300 mg and 57 mg per 100 cc, respectively. A gram stain of the spinal fluid revealed many gram-negative diplococci in pairs. A blood culture was positive for meningococci. Treatment with sulfadiazine, instituted shortly after admission, resulted in a rapid fall in the temperature and clearing of the signs of meningeal infection, and the patient was discharged completely cured 37 days after admission.

She remained in a fair state of health, with recurring edema of the face and ankles, occasional slight headaches and per-

sistent anemia, hematuria and albuminuria, for the next 7 months, and carried out her duties as a salesgirl.

On November 14, 1944, or 237 days after the onset of the first attack of meningitis, the patient was admitted to the Haynes Memorial Hospital. During the previous 2 weeks she had developed a "head cold" with associated headache. During that time, the temperature ranged from 99 to 101°F and there were mild migratory joint pains involving the wrists, knees and elbows. Three days prior to entry, the patient noted some "red spots" on her legs, but had no further difficulty until the afternoon of the day of admission, when she had a sudden onset of a hard, shaking chill and a severe headache, with a rise in temperature to 104°F and delirium.

Physical examination on admission revealed a well developed, well nourished girl, appearing acutely ill and markedly delirious. The temperature was 100.4°F, the pulse 130, the respirations 24, and the blood pressure 130/70. There were a few pink macular areas scattered over the skin of the back and abdomen. The head was essentially normal. The pupils were round, regular and equal and reacted to light. There was a moderate degree of papilledema of both optic disks. The neck was markedly stiff. The lungs were clear on percussion and auscultation. Examination of the heart revealed no enlargement on percussion, the sounds were of good quality and the rhythm was regular. A Grade II systolic murmur was heard with greatest intensity over the mitral area but was not transmitted toward the axilla. The aortic second sound was greater than the pulmonic. The abdomen revealed no masses, spasm or detectable tenderness. The liver, spleen and kidneys were not palpable. The Kernig and Brudzinski signs were strongly positive bilaterally, and all the superficial and deep reflexes were markedly hyperactive but equal.

The urine on admission had a specific gravity of 1.020 and gave a +++ test for albumin; the sediment contained innumerable white cells and 40 to 100 red cells per high-power field. The white-cell count was 18,000, with 82 per cent neutrophils, of which 21 per cent were band forms, 12 per cent lymphocytes, 5 per cent monocytes and 1 per cent eosinophils. Lumbar puncture carried out immediately after admission revealed an initial pressure equivalent to 350 mm. of water, with a normal rise and fall on jugular and abdominal compression. The spinal fluid contained 3230 cells per cubic millimeter, 95 per cent of which were polymorphonuclear leukocytes, and 21 mg of sugar, 97 mg of protein and 691 mg of chloride per 100 cc. A gram stain revealed many intracellular gram-negative biscuit-shaped diplococci, and a culture yielded organisms that were identified as *N meningitidis*, Type 1. Several blood cultures were sterile.

Because of the presence of moderately severe chronic renal disease and the risk of drug intoxication, the patient was treated with penicillin instead of one of the sulfonamides, being given 15,000 units intramuscularly every 3 hours for 10 days. In addition, 20,000 units was administered intrathecally on the 1st day and 40,000 units by the same route on the 2nd day. The temperature fell rapidly and reached a normal level on the 6th hospital day, at which time there was no evidence of delirium but signs of meningeal irritation were still present. Recovery was rapid, and on the 9th hospital day the cerebrospinal fluid contained only 57 lymphocytes per cubic millimeter and normal quantities of sugar, protein and chloride. A culture was negative.

Numerous examinations of the urine and studies of the chemical constituents of the blood established a diagnosis of chronic glomerulonephritis without azotemia or hypertension but with persistent hematuria, albuminuria and hypoproteinemia. The patient was kept in the hospital for 7 weeks after she had completely recovered from the meningitis for further investigation of the renal disease. There was no sign of reinfection of the meninges during this period. There was no evidence of an exacerbation of the glomerulonephritis during the course of the meningococcal infection.

On July 9, 1945, the patient was readmitted after having had a sore throat and fever for 2 days and four shaking chills with an elevation of temperature to 101°F on the day prior to entry. Physical examination revealed diminished resonance to percussion over the right upper lobe posteriorly, where there were heard many fine, moist rales. X-ray examination of the lungs revealed pneumonia of the right upper lobe.

The patient was treated with 120,000 units of penicillin a day for 8 days and made an uneventful recovery. Throat cultures revealed the presence of *N meningitidis*, Type 1.

the bladder (Fig 8) In pelvic trauma the bladder may be spared and the injury may be confined to the urethra (Fig 9)

From the foregoing, it is concluded that retrograde urethrocytography is an extremely accurate procedure if simple precautions are taken to avoid sources of error For these reasons, this should be a routine procedure in cases of suspected trauma of the lower urinary tract in which a definite diagnosis cannot be established by clinical examination

### SUMMARY AND CONCLUSIONS

Seven cases of traumatic rupture of the bladder and posterior urethra are described

The diagnosis in these cases was established by retrograde urethrography and cystography with a radio-opaque contrast medium

A number of roentgenologic signs are described

that permit the differential diagnosis of intra peritoneal and extraperitoneal injuries

Certain fallacies of excretory and retrograde cystograms are pointed out

It is concluded that retrograde urethrocytography is a simple, safe and accurate method in the detection of trauma of the lower urinary tract

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## RECURRENT MENINGOCOCCAL MENINGITIS\*

### Report of a Case

LOUIS WEINSTEIN, M D,† AND EDITH D STANLEY, M D ‡

BOSTON

THE incidence of relapse in the course of meningococcal meningitis before the use of the sulfonamides in its treatment was about 50 per cent Since the universal adoption of this group of drugs as the therapeutic measure of choice, the relapse rate has dropped to only 8 per cent<sup>1</sup> True recurrence of this disease, on the other hand, is a rare phenomenon

For the purpose of discussion, it is important to differentiate a relapse from a true recurrence The former is defined in *Gould's Medical Dictionary*<sup>2</sup> as "a return of an attack of a disease shortly after the beginning of convalescence" The latter has been characterized by Schaffer and Freeman<sup>3</sup> as "a fresh infection, a second attack, a repetition of the whole disease syndrome" Thus, a recurrence presupposes the passage of an appreciable period of time during which the patient is free of all symptoms of the original disease and, in many cases, has returned to normal activity By definition, it can occur only after the convalescent period has ended

Only a few well substantiated recurrences of meningococcal meningitis have been reported in the literature In 1919, Herrick and Dannenberg<sup>4</sup> studied 4 patients who, after apparently having made a complete recovery from a first attack of this

disease, were victims of a second infection with the same organism after intervals of twenty-four, forty-three, one hundred and four and one hundred and forty-three days, respectively Bacteremia was present in each case during the second episode Rémond and Colombiès<sup>5</sup> have described the case of a twenty-year-old medical student who had two attacks of meningococcal meningitis separated by a symptom-free period of eight months and completely recovered from each of them A case of recurrence seven months after the initial episode of infection of the meninges with *Neisseria meningitidis* has been reported by Christie<sup>6</sup>

A second attack of meningococcal meningitis may be due to invasion by the same serologic type as the one that was responsible for the first episode or a different one The source of the organisms causing the new infection may be a carrier or the patient himself, in the latter instance, the bacteria may be present in the pharynx or on damaged heart valves for long periods of time without producing any symptoms An example of a recurrence resulting from contact with a carrier of *N meningitidis* has been reported by Brewis,<sup>7</sup> who described a patient who made good recoveries after two attacks of meningococcal meningitis separated by a period of four years, the second illness was treated with sulfonamides A possible case of a second attack in which the pharynx of the patient himself appeared to be the source of the infecting organisms was studied by Räuber<sup>8</sup> This patient suffered two

\*From the Evans Memorial and Haynes Memorial Massachusetts Memorial Hospitals and the Department of Internal Medicine Boston University School of Medicine

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†Assistant professor of medicine, Boston University School of Medicine  
visiting physician Haynes Memorial Massachusetts Memorial Hospitals  
‡Assistant in medicine Boston University School of Medicine.

## THE DANGERS OF MODERN INSULIN SYRINGES\*

WILLIAM S COLLENS, M D,† LOUIS C BOAS, M D,‡ AND JAMES D ZILINSKY, M D §

BROOKLYN, NEW YORK

SINCE the discovery of insulin, a situation has existed in connection with the syringe employed for its administration that has never been satisfactory. The original introduction of a variety of insulin concentrations necessitated the construction

Apparently, in an attempt at economy, syringes with double graduations were manufactured. Thus, to provide syringes for the injection of insulins of U 10, U 20, U 40 and U 80 strengths, the manufacturer supplied a U 10-20 syringe,—used for

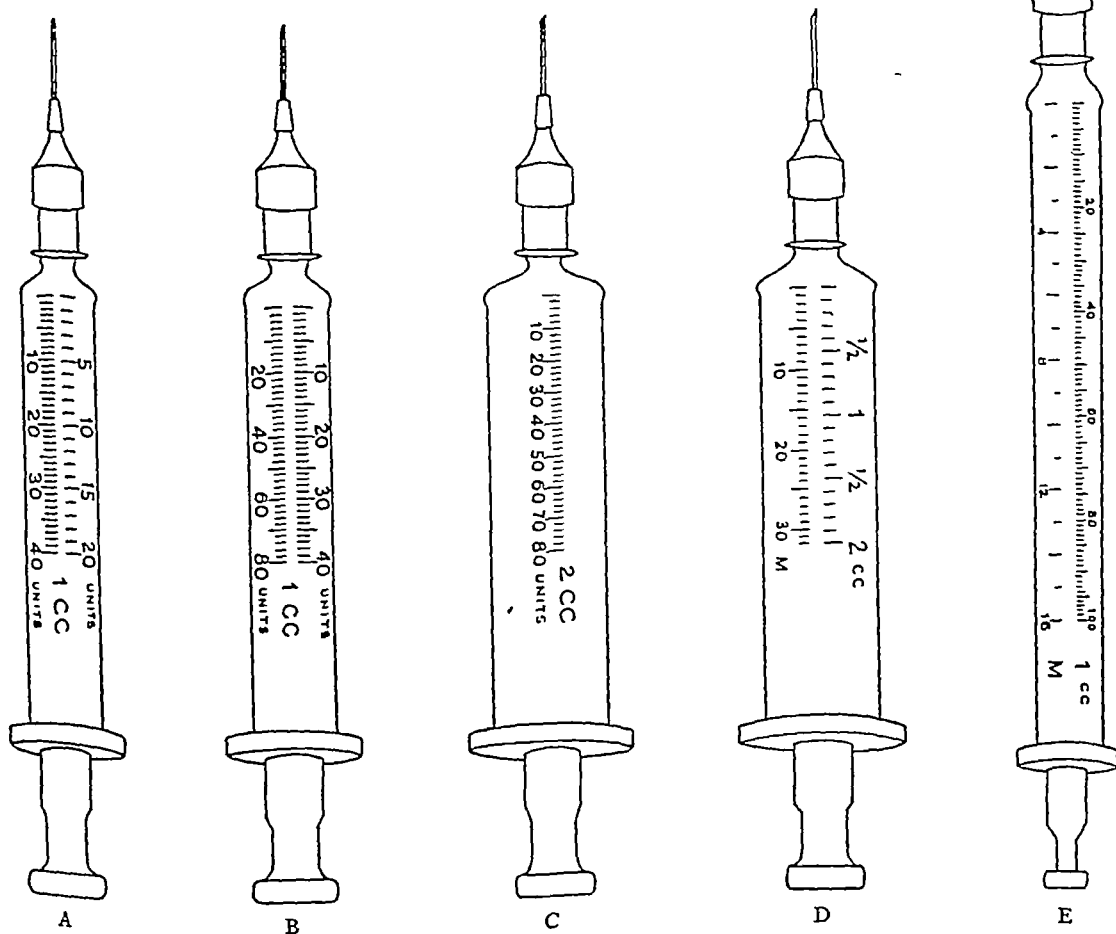


FIGURE 1

of hypodermic syringes with different calibrations corresponding to these various concentrations

\*From the Department of Metabolism, Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases

†Chief, Diabetic Clinic, and associate visiting physician Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases

‡Assistant, Diabetic Clinic, and assistant in Department of Metabolism Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases

§Assistant, Diabetic Clinic, and assistant in Department of Metabolism Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases

U 10 and U 20 insulin,—a U 20-40 syringe—used for U 20 and U 40 insulin—and a U 40-80 syringe—used for U 40 and U 80 insulin (Fig 1A and B). It has always been our opinion that the dual calibrations on the syringe serve to confuse the majority of diabetic patients and present a serious obstacle to the successful administration of the dose of insulin planned by the physician. In recent years, this problem has been further

Blood cultures were sterile. The patient was discharged completely recovered from the pneumonia 16 days after admission. The status of the renal disease was not altered by the pulmonary infection.

Bacteriologic examination of the pharynx on two occasions after the last discharge did not reveal the presence of meningococci.

### DISCUSSION

This patient had chronic diffuse glomerulonephritis in the nephrotic stage and suffered two attacks of meningococcal meningitis during a period of seven months. The source of the bacteria that produced the two episodes of disease is unknown. Meningococcal meningitis was epidemic at the time of the first attack, in the spring of 1944, but only rare cases of this disease were occurring in this area at the time of the recurrence, in November, 1944. It is interesting, however, that the two episodes of meningitis occurred in the early spring and late fall, when the incidence of meningococcus carriers is apt to be high, and it is likely that a carrier was the source of infection. It does not appear probable that the recurrence was due to organisms present in the pharynx during the symptom-free period of seven months, since these organisms were not isolated from the throat during the second attack. The discovery of meningococci in the pharynx many months after recovery from the second episode of meningeal infection suggests a chronic carrier state. It is possible that these bacteria were present in extremely small numbers while the patient was well, increased during the bout of pneumonia and again disappeared.

The question of the relation of the nephrotic stage of the chronic diffuse glomerulonephritis to the increased susceptibility to bacterial infection is an interesting one, but no concrete evidence for a causal

connection between the two is at hand. Whether an analogy can be drawn between lipid nephrosis and the nephrotic state of chronic glomerulonephritis with respect to decreased resistance to infection is difficult to say. The repeated bacterial infections produced no exacerbation of the chronic renal disease.

### SUMMARY

True recurrences of meningococcal meningitis are rare.

A case of chronic glomerulonephritis in which there were two attacks of meningococcal meningitis in seven months is described.

The question of the role of the nephrotic phase of chronic glomerulonephritis in increasing susceptibility to bacterial infection is raised.

Three episodes of severe bacterial infection exerted no noticeable effect on the course of chronic glomerulonephritis in the case reported.

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THE DANGERS OF MODERN INSULIN SYRINGES\*

WILLIAM S COLLENS, M D, † LOUIS C BOAS, M D, ‡ AND JAMES D ZILINSKY, M D §

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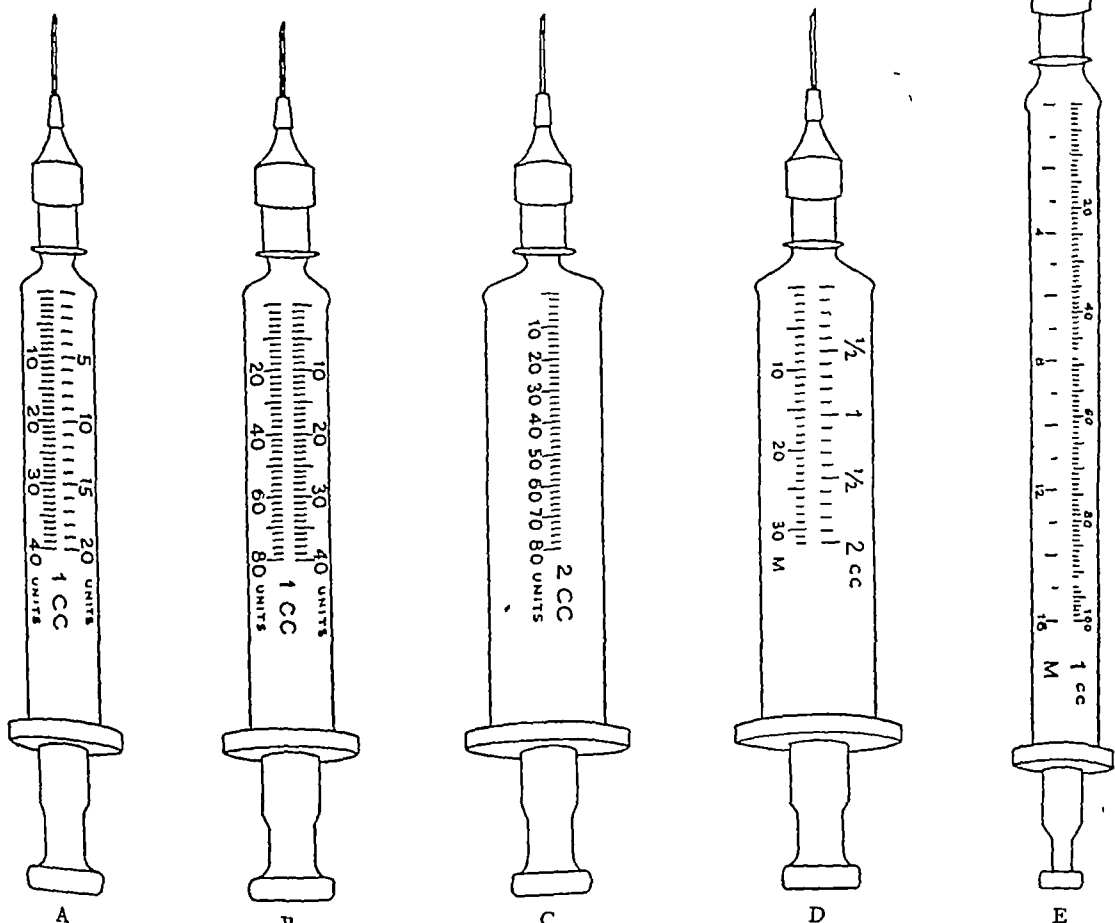


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U 10 and U 20 insulin, — a U 20-40 syringe — used for U 20 and U 40 insulin — and a U 40-80 syringe — used for U 40 and U 80 insulin (Fig 1A and B). It has always been our opinion that the dual calibrations on the syringe serve to confuse the majority of diabetic patients and present a serious obstacle to the successful administration of the dose of insulin planned by the physician. In recent years, this problem has been further

\*From the Department of Metabolism, Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases  
†Chief Diabetic Clinic, and associate visiting physician, Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases  
‡Assistant, Diabetic Clinic, and assistant in Department of Metabolism, Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases  
§Assistant, Diabetic Clinic, and assistant in Department of Metabolism, Israel Zion Hospital and the Jewish Sanitarium and Hospital for Chronic Diseases

complicated by the introduction of modified forms of insulin, such as protamine-zinc insulin, zinc insulin crystals and globin insulin. The introduction of a new technic for administering insulin mixtures has still further aggravated the problem.

It may be of interest to enumerate the variety of syringes that are sold to diabetic patients for the administration of insulin. They are as follows: a 1-cc syringe graduated in units, for use with U 10 and U 20 insulin, a 1-cc syringe graduated in units, for use with U 20 and U 40 insulin (Fig 1A), a 1-cc syringe graduated in units, for use with U 40 and U 80 insulin (Fig 1B), a 2-cc syringe graduated to 80 units, for use with U 40 protamine-zinc insulin (Fig 1C), a 2-cc syringe graduated to 80 and 160 units, for use with U 40 and U 80 protamine-zinc insulin, a 2-cc syringe graduated in tenths of a cubic centimeter and minims (Fig 1D), a 1-cc tuberculin-type syringe graduated in hundredths of a cubic centimeter (Fig 1E), and a 1-cc tuberculin-type syringe graduated in tenths of a cubic centimeter.

Insulin is generally administered either by the patient himself or by some member of his family, a neighbor, a practical nurse or a registered nurse. Only occasionally is it given by the physician. Although the latter can adapt himself to the use of a syringe of any type, it is difficult to avoid confusion in dosage when such a large variety of syringes is easily available to anyone else giving the injection, including the trained nurse. This statement is made as the result of practical experience and observation of the errors that have been made in the administration of insulin.

We know of patients using U 40 insulin who read their dose on the U 20 scale of a U 20-40 syringe. Thus, although the physician might have ordered the injection of 15 units of insulin, it is readily seen that the taking up of U 40 insulin to the "15" mark on the U 20 scale would actually result in a dose of 30 units. This happens to be the most frequent type of error. It appears that the reason for it is that the graduations on the U 20 scale are wider and the figures are larger than those on the U 40 scale, thus making them more easily seen, especially by a patient whose vision is not particularly good.

One of the most dangerous errors in the administration of insulin occurs when a patient uses an ordinary hypodermic syringe graduated in cubic centimeters and minims (Fig 1D). We recall a patient who appeared for the first time with the chief complaint of frequent insulin reactions. She had been diabetic for five years and had taken insulin for three years. She had apparently encountered difficulty in controlling her glycosuria and had changed from U 40 insulin to U 80 insulin, because, she said, U 80 insulin was "stronger." She had also been advised by her physician to change from unmodified insulin to protamine-zinc

insulin. Inquiry into the type of syringe employed revealed that she was using an ordinary 2-cc hypodermic syringe. Although she stated that she was taking "24 units" of protamine-zinc insulin, she was in fact receiving 24 minims. The latter amount is approximately equivalent to 1.5 cc, and in terms of U 80 insulin it is evident that this patient was taking 120 units of insulin. Her hypoglycemic

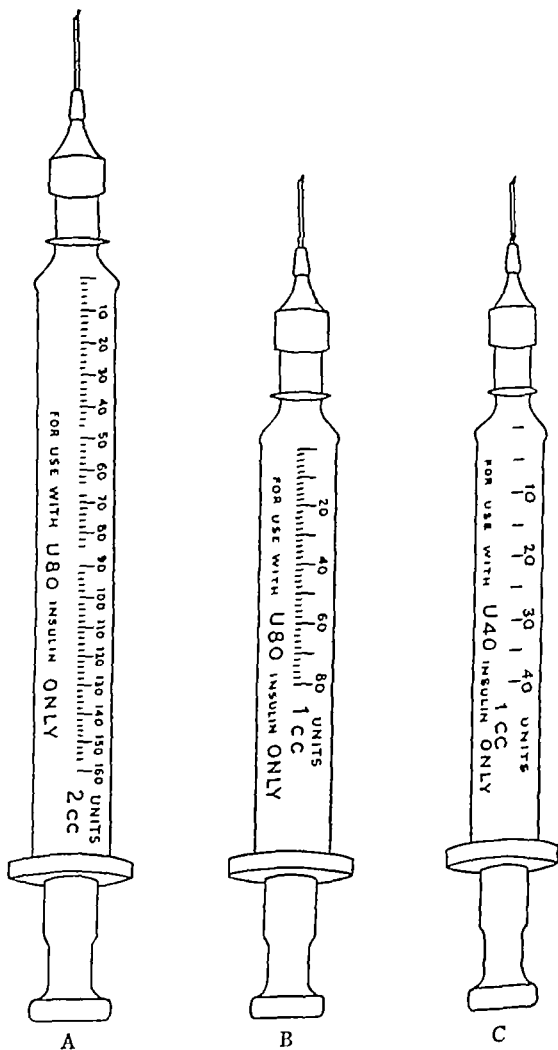


FIGURE 2

reactions therefore caused little surprise when it was ultimately found that the daily insulin requirement for the satisfactory control of her diabetes was only 45 units.

A registered nurse who was diabetic was taking U 80 protamine insulin up to the "35" mark on the 40-unit scale of a U 20-40 syringe. She assumed that she was injecting 35 units when in reality she was injecting 70 units.

It is evident that such practices can result only in accidents from the toxic effects of insulin overdosage. These errors are made largely because of the fact that the instruction in insulin administra-

tion is too haphazard. The physician frequently fails to recognize that successful therapy is predicated on adequate and painstaking instruction. Teaching the technic of proper insulin administration should not be left to an inexperienced attendant or a neighbor or relative of the patient who happens to be taking insulin. The patient can with only a little effort be taught the exact technic for the proper administration of the kind and dose of insulin he should receive.

Simplification in the administration of insulin can be achieved, first, by the elimination of U 10 and U 20 strength insulin from the market, which has been recommended by the American Diabetes Association. If this were done, only two concentrations of insulin, U 40 and U 80, would be available. The most effective remedy, however, would be the elimination of the insulin syringe with dual markings. Only two types of syringes should be available to the patient—one with a single scale graduated to 40 units and to be used with U 40 insulin only (Fig 2C), and the other graduated for U 80 insulin only (Fig 2A and B). The syringe with calibrations for U 40 insulin should be manufactured in the 1-cc. size only. Those employed for the administration of U 80 insulin should be made in 1-cc. and 2-cc. sizes, with the former calibrated to 80 units and the latter to 160 units. The 2-cc. syringe is recommended for patients who take insulin in doses greater than 80 units. It is also useful for patients to whom insulin mixtures are given, with the total

dose of unmodified and protamine-zinc insulin exceeding 80 units.

To emphasize further the separate identity of these syringes, the graduations and lettering of the U 40 syringe should be etched in red to conform with the red label and cap of the U 40 insulin vial, and the U 80 syringes should be etched in green to conform with the label and cap of the U 80 insulin vial. To ensure further against the possibility of error, the printed matter on both the syringe and the cardboard container in which it is sold should read, "This syringe is to be used for U 40 insulin only" and "This syringe is to be used for U 80 insulin only," respectively.

It is suggested that when physicians find that they must prescribe more than 40 units of insulin in a single dose, they recommend the use of U 80 insulin only, and that when this change is made the patient be instructed to use only a U 80 insulin syringe. In the meantime, until the manufacturers can be persuaded to produce syringes according to the recommendations made herein, physicians should prescribe only the U 40-80 syringe and impress the patient with the importance of employing the appropriate scale for the insulin ordered.

#### SUMMARY

The confusion caused by insulin syringes with dual calibrations is pointed out.

Recommendations are made for the manufacture of syringes with simplified graduations to eliminate the possibility of error in dosage.



## CLINICAL NOTE

## ARTERIOVENOUS ANEURYSM OF THE GREAT VESSELS OF THE NECK

## REPORT OF A CASE

COLONEL PHILLIPS L. BOYD, MC, AUS\*

**A**RTERIOVENOUS aneurysms and fistulas are lesions of comparative rarity, even in wartime. The incidence of these vascular injuries in this general hospital in the European Theater of Operations has been 1 in every 500 admissions. All the cases except the one reported herein occurred in the vessels of an extremity.

The problems of diagnosis and of the determination of adequate collateral circulation prior to surgical intervention have been well covered by Lewis and Drury,<sup>1</sup> Wise,<sup>2</sup> Waugh,<sup>3</sup> Pemberton and Black<sup>4</sup> and King.<sup>5</sup> The following case of arteriovenous aneurysm involving the internal carotid artery and internal jugular vessels is reported because of the technical complications inherent in its location and because of the excellent surgical result obtained.

## CASE REPORT

A 35-year-old, German soldier was wounded in action near Paris on August 23, 1944, and sustained penetrating wounds of the left wrist from fragments of high-explosive shell, with a compound comminuted fracture of the distal end of the radius and ulna and wounds of the right upper arm and shoulder and right side of the neck at the level of the thyroid cartilage.

At the forward medical installations, the wounds were debrided and dressed and the fractured wrist was immobilized in a cast. Sulfonamides, penicillin and 1500 units of tetanus antitoxin were administered. Four days later, at a transit hospital, it was noted that a pulsating mass had appeared on the right side of the neck at the level of the thyroid cartilage. It was thought that an arteriovenous fistula was present and that an arteriovenous aneurysm might be developing.

On admission to this hospital on September 6, 1944, the patient was ambulatory. The voice was husky and hoarse. The left wrist and forearm were in a cast, and the wounds were healing well. Physical examination revealed a mass 2.5 by 3.0 cm. in diameter on the right side of the neck just lateral and superior to the thyroid cartilage, with slight visible pulsation, a marked tactile thrill and a loud auscultatory bruit, which was transmitted along the great vessels into the base of the neck and out along the supraclavicular vessels on the right. Neurologic examination showed a Horner's syndrome on the right and paralysis of the right vocal chord. The wrist was poorly reduced, and there was considerable loss of motion.

X-ray examination on September 14 revealed a fragment of metal measuring 0.5 by 0.5 by 0.2 cm. just lateral to the right side of the superior border of the fifth cervical vertebra. A film of the left wrist showed the fracture to be poorly reduced. Further studies with compression of the mass by digital pressure indicated that the circle of Willis and the cerebral collateral vessels could probably maintain adequate circulation to the cerebrum. Studies of the blood pressure in the right and left arms were not done. Inasmuch as the mass was constantly enlarging and it was impossible to maintain adequate local compression, it was decided to excise the lesion. Cardiac studies showed no change in its size.

\*Instructor in surgery, Boston University School of Medicine and assistant in surgery, Massachusetts Memorial Hospitals (on leave of absence).

On September 19, 4 weeks after injury, operation was performed under gas, oxygen and ether anesthesia. A downward incision was made from the mastoid process to the clavicle along the anterior margin of the right sternomastoid muscle. The carotid sheath was opened at the level of the isthmus of the thyroid gland, the common carotid artery and internal jugular vessels were isolated, and the artery was slowly compressed with a clamp, 45 minutes being required before closure was complete. Exploration of the mass revealed that it was an aneurysmal sac occupying the middle three fifths of the sternomastoid muscle (Fig. 1). The mass

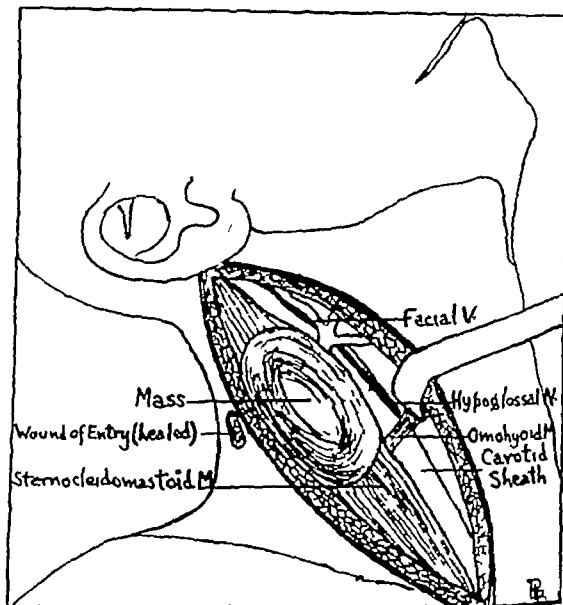


FIGURE 1 Aneurysmal Mass Uncovered in Right Side of Neck

was contained only by the attenuated fibers of this muscle and its fascial sheath and by the platysma muscle. In an effort to open the carotid sheath above the mass, the sac was ruptured, and from then on bleeding was controlled by digital pressure. The common carotid artery and internal jugular vein were ligated proximal to the lesion. After considerable difficulty, the internal jugular vein was ligated distally nearly at the level of its emergence from the skull. A double ligature was then passed around the internal jugular and internal carotid vessels distal to the lesion. All bleeding ceased, and the aneurysmal wall, which consisted of friable muscle tissue lined with a glossy endothelial layer, was dissected out. The arteriovenous fistula (Fig. 2) had developed between the internal carotid artery and the internal jugular vein at a point 1 cm. beyond the bifurcation of the common carotid artery.

The small metallic foreign body (Fig. 2) had completely traversed the carotid sheath at the level of the thyroid cartilage, injuring the wall of the internal carotid artery and internal jugular vein, completely transecting the vagus nerve—causing a spindle-shaped neuroma 0.3 cm. in diameter—and injuring the cervical sympathetic trunk. The foreign body could not be palpated and was not removed. The wound was closed in three layers with a rubber-dam drain, which was brought out at the inferior angle of the wound.

During the operation the patient was supported by the intravenous injection of 500 cc. of plasma, 1500 cc. of stored whole blood and 500 cc. of glucose in saline solution. The entire operation lasted for 3 hours. The patient was returned to the ward in good condition.

The patient was stuporous for 48 hours postoperatively but rallied quickly. On the 14th postoperative day, he was up and about. The wound was discharging a slight amount of seropurulent material. No evidence of cerebral damage could be detected. The Horner's syndrome and the paralysis of the right vocal chord persisted, although the voice was stronger and less husky, probably owing to the release of

pressure on the larynx. The wrist had to be reset, but even after this step there was considerable loss of motion. The patient was able to perform routine work details and was evacuated to a prisoner-of-war camp 6 weeks postoperatively, in excellent condition.

As a general policy, early operation in cases of arteriovenous fistula or aneurysm is not necessary. In fact, many surgeons believe that it may be unwise, since adequate collateral circulation has not had time to develop. Lewis and Drury,<sup>1</sup> in their excellent study, state their opinion that the alterations that occur in the part of the vascular tree

aneurysms in 3 German prisoners of war were successfully operated on within one month of the injury. In cases in which distal pulsations are present, further study with digital pressure over the involved point must be accomplished, and observation of the color and temperature changes of the limb must be made.

King<sup>5</sup> has reported a case closely similar in location to the one described above. It was also treated by ligation above and below the lesion, eight weeks after injury, during which time the patient developed cardiac enlargement and blood-pressure changes. In the present case, operation was performed four weeks after injury, and so far as could be detected no cardiac changes occurred.

It is the policy in this theater to refer most cases of arteriovenous aneurysm or fistula to the Zone of the Interior for operation. In rapidly developing lesions of the great vessels of the neck or thorax, however, surgical control is often inadequate and cardiac changes may develop early. With a proper understanding of the technical complications, early operation can be successfully performed, and it offers the only chance of cure and avoidance of cardiac damage.

#### SUMMARY

An unusual case of arteriovenous aneurysm of the great vessels of the neck is reported. Although operation was considered necessary four weeks after injury, the patient made a rapid and complete recovery.

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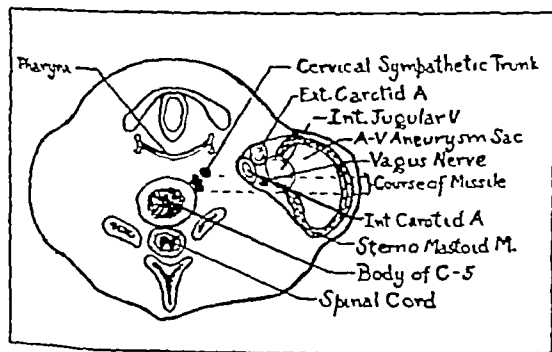


FIGURE 2 Cross Section at the Level of the Fifth Cervical Vertebra Indicating the Course of the Missile and the Structures Injured

peripheral to a fistula are such that if from the start there is no evidence of gross circulatory failure, surgical interference with a large vessel, a procedure that in ordinary circumstances might lead to serious complications, can be undertaken with impunity. Most of the peripheral aneurysms seen in war wounds on this service have shown a loss of distal pulsation but have had evident adequate distal circulation. A case requiring amputation for circulatory gangrene showed an arteriovenous aneurysm of the popliteal vein and artery. Operation, therefore, in the average case in no way seriously alters the vascular balance of the limb. Such

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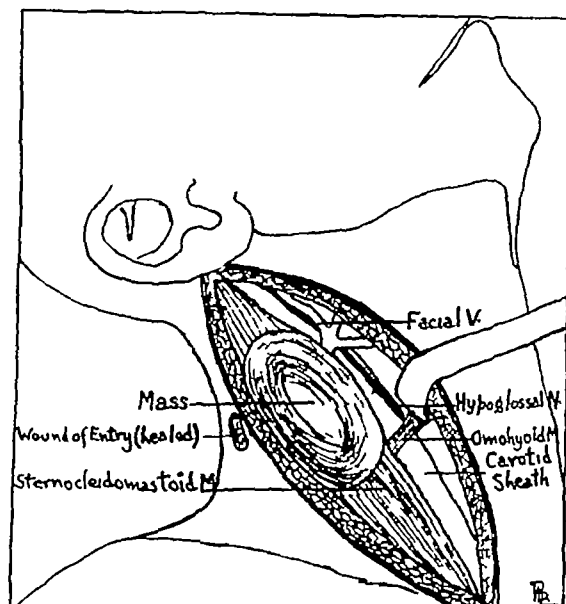


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ture Increased fever and prolonged febrile response to typhoid vaccine can be obtained by the concomitant use of a covered cradle containing electric-light bulbs<sup>46</sup> The reported results are encouraging, especially when combined with chemotherapy

A report on the use of thiamine by spinal injection for the relief of the pains of tabetic crises<sup>47</sup> seems encouraging enough to warrant further study

### *Intensive Therapy*

The various types of massive-dose technic that have been under study for the last twelve years are still undergoing refinement The United States Army hospital installations in the European Theater of Operations carried out treatment by the twenty-day multiple-syringe injection technic<sup>48</sup> Patients were hospitalized during this time, many received a course of ten bismuth injections after discharge from the hospital Reactions encountered were comparable to those previously experienced with this type of treatment Although follow-up of the patients was incomplete, the results appeared extremely satisfactory for periods of four to six months Only 1 of 205 patients with seronegative primary syphilis showed a doubtful serologic reaction four months or more after treatment The subsequent use of penicillin therapy interrupted this program

MacKee and Astrachan<sup>49</sup> treated 61 patients by the method of Eagle and Hogan,<sup>50, 51</sup> which consists of tri-weekly injections of Mapharsen for twelve weeks, combined with one bismuth injection each week These authors find this to be an efficacious method, with fewer reactions than the intravenous drip treatment, but caution that it is still in the experimental stage Less encouraging results have been observed by others<sup>52</sup> with a slightly less intensive schedule A daily injection of Mapharsen for thirty days, without bismuth, resulted in only 51 per cent seronegative reactions among 62 patients with early syphilis A four-year experience with the five-day-drip method has also been reported<sup>53</sup> One hundred patients were treated, but only 50 were followed up for periods of one to three or more years Only 4 cases are classified as treatment failures There was 1 fatality, which was due to hemorrhagic encephalitis

Further observations on the one-day treatment of syphilis with fever and Mapharsen have appeared<sup>54</sup>, 421 patients with early syphilis are included They were treated by several schedules, including the administration of Mapharsen during the induction period, before and after the fever and at its termination The best results were obtained among the 206 patients so treated after the termination of fever These were observed for three to nine months, only 16 (8 per cent) showed a clinical relapse, and only 5 (2 per cent) a serologic relapse Only forty-eight hours of hospitalization was required The cost per case was estimated at \$30

A word of caution concerning the rapid treatment

of early syphilis during pregnancy should be carefully noted One of a series of 43 pregnant patients with early syphilis died of encephalopathy<sup>55</sup>

The United States Public Health Service<sup>56</sup> has published its evaluation of massive arsenotherapy The data were taken from 4351 cases treated at twenty-two clinics by six varied plans The best results exclusive of the highly reactive intravenous-drip technic with neoarsphenamine, followed the use of multiple-syringe injections of Mapharsen combined with typhoid vaccine This yielded satisfactory results in 85 to 90 per cent of the cases of primary syphilis and in 70 per cent of those of secondary syphilis Relapse occurred in 5 to 6 per cent of the primary cases and 10 to 13 per cent of the secondary cases The administration of bismuth during the period of treatment appeared to improve the results Acute encephalopathy was observed in 31 cases (0.71 per cent), and nearly half of these patients died

### REACTIONS TO TREATMENT

#### *Bismuth*

Heyman<sup>57</sup> has presented a review of the literature on bismuth poisoning and reports observations on 4 patients with severe systemic manifestations and renal insufficiency following bismuth therapy Bismuth melanosis of the large intestine and bismuth cervicovaginitis occurred in 2 cases The author believes that these conditions occur oftener than has been reported The renal lesions in these patients were closely similar to those produced in animals by experimentation In all 4 patients, the nephrotoxic action of the drug produced an intensification of pre-existing renal insufficiency In 2 of them, the effect was temporary and a fair degree of renal function returned in a few months, death resulted in the others It is obvious that great caution is necessary with the use of bismuth in patients who already have some renal damage

Dental examination of approximately 500 soldiers receiving bismuth treatment for syphilis revealed that 70 per cent of them had some gingival manifestation of bismuth deposit<sup>58</sup> The condition appeared chiefly in the patients who had failed to practice oral hygiene The bluish-black line is first seen at the site of any pre-existing inflammation The standard dose of 0.13 to 0.20 gm of bismuth salicylate, it is stated, should cause little or no disturbance if oral hygiene is good, provided that injections are not extended beyond a series of twelve to fifteen treatments Only in cases of gross negligence or intolerance to bismuth does a severe stomatitis develop

#### *Post-Arsphenamine Jaundice*

Beattie and Marshall<sup>59</sup> discuss the etiology of post-arsphenamine jaundice It is stated that although the organic arsenicals used in the treatment of syphilis are hepatotoxic, there are indica-

## MEDICAL PROGRESS

### SYPHILIS (Concluded)

G MARSHALL CRAWFORD, M D \*

BOSTON

#### THERAPY

The use of penicillin in the treatment of syphilis has developed with an explosive force almost analogous to that of the atomic bomb. The literature on this particular phase of the treatment of syphilis is so voluminous as to warrant a completely separate category. Consequently, it will be discussed in a separate section of this progress report.

Moore<sup>42</sup> has given a most instructive discussion of the chemotherapy of syphilis from the time of the first knowledge of the disease. This covers a period of four hundred and fifty-one years, which is divided into three main periods according to the advances made in chemotherapeutics. The first dates from 1493 to 1903, during which time little was accomplished. From 1903 until 1943, great gains were made, including the discovery of the causative agent of syphilis, the serologic test for syphilis and the use of bismuth, massive-dose technic, hyperpyrexia and combined-treatment programs. The last period of course begins with the advent of penicillin. The accomplishments of this drug up to the time of writing are adequately reviewed, and the limitations of the present knowledge are carefully pointed out. Moore stresses the fact that with all types of syphilotherapy it has taken some time to work out the optimal time-dose relation. This is obviously as true of penicillin as it is of older forms of treatment. Moore believes that penicillin, in combination with an arsenoxide, may prove to be more effective than either drug alone, and outlines the dose schedules that are under trial at the present time. He stresses the fact that the late results of any of the intensive methods of therapy will not be available for another generation. This point has been repeatedly emphasized in these columns during the last few years.

#### Oral Bismuth

Barnett and Meininger<sup>43</sup> have published a follow-up report on the use of oral bismuth medication in the form of so-called "sobisminol mass." There are several categories of patients in which oral treatment for syphilis is particularly useful. These include those unable to consult a physician at regular intervals owing to occupation, isolated residence, inadequate transportation and so forth. Tertiary syphilis associated with chronic invalidism

is another indication for oral treatment. There are also some patients who refuse parenteral therapy for various reasons. Sobisminol mass alone is not recommended for the treatment of early syphilis, but it may be substituted for bismuth by injection in conjunction with arsenotherapy if necessary. In late syphilis, sobisminol mass produced a rapid involution of gummatous lesions, and a number of patients with advanced cardiovascular involvement and neurosyphilis were symptomatically improved by its administration. The toxicity of sobisminol mass is low. One third of 400 patients experienced mild gastrointestinal disturbances, but in less than one fifth of these was it necessary to discontinue the drug. Although one may now hope for therapeutically efficient oral penicillin, this work with oral bismuth should not be entirely forgotten.

#### Neurosyphilis

Solomon, Moore, O'Leary, Stokes and Thomas<sup>44</sup> outline the treatment methods recommended for the various forms of neurosyphilis to obtain the maximum benefit of treatment that can be secured by hospitalization in a general hospital, not to exceed three months. They divide neurosyphilis into nine groups for the purpose of therapy, and outline the most desirable form of treatment for each. Chemotherapy is advocated following fever therapy in most cases, as soon as malaria is terminated and during convalescence from this infection. Injections of Mapharsen (0.06 gm) are to be given daily for ten days. The need of subsequent chemotherapy is determined by observation of the case in hand. Here again, the results of penicillin therapy may warrant changes.

The simpler method of inducing hyperpyrexia by intravenous drip with triple-typhoid vaccine should not be overlooked. Although not all patients achieve a satisfactory febrile response to this treatment, it is often usable in cases in which malaria is not well tolerated. In a series of 60 cases of various types of neurosyphilis treated by this method, there was a satisfactory response in early paresis and in asymptomatic neurosyphilis.<sup>45</sup> The advantages of this method of hyperpyrexia over malaria in a general hospital include shorter hospitalization, greater convenience, greater ease of administration and better control of the tempera-

\*Instructor in dermatology. Harvard Medical School assistant dermatologist, Massachusetts General Hospital.

syphilis is a disease in which penicillin has been found to be an effective agent, but that its position has not been definitely defined and will require additional experimental work

#### *Effect on Treponema pallidum*

It has been demonstrated that *Treponema pallidum* can become resistant to penicillin<sup>70</sup> The work was done with experimental infection of rabbits, which were given sufficient penicillin to modify the course of the disease but not enough to effect a cure. This resulted in the development of a penicillin-fast strain, which persisted after further animal passages. This emphasizes the necessity for adequate treatment with penicillin in clinical cases. It has further been shown that although a single dose of penicillin may sterilize an infectious lesion, even an extremely high single dose is not sufficient to cure experimental syphilis in rabbits<sup>71</sup> This is a good example of the importance of the time-dose relation.

Dunham and Rake<sup>72</sup> report the results of experiments performed in vitro and in vivo to determine the relative activity of partially purified penicillin and of crystalline penicillin G on *T. pallidum*. Crystalline penicillin G in a high concentration had little or no effect on the motility of the organism in vitro. Under the same conditions, a solution containing one fourth as much of the least pure penicillin preparation employed in these studies immobilized all the spirochetes. *T. pallidum* exposed to certain partially purified preparations of penicillin was noninfectious for rabbits, whereas spirochetes similarly exposed to crystalline penicillin G produced orchitis. It was demonstrated, however, that crystalline penicillin G had some antisyphilitic action. It failed to protect rabbits against infection of syphilis unless given in tremendous doses, whereas partially purified penicillin protected a large proportion of rabbits when small doses were given.

#### *Prolongation of Action*

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and Neo-Syneprine, together with gelatin have been shown to prolong the action of penicillin. A combination of dextrose with a vasoconstrictor has also been found to furnish a satisfactory and harmless extension of action.<sup>80</sup> Zinnamon<sup>81</sup> studied the retardation of intramuscular absorption of penicillin combined with aluminum hydroxide, pectin, globin and various fixed oils. The fixed oils effected the most retardation, a mixture of beeswax and sesame oil being the most satisfactory. The use of pitressin subcutaneously to produce oliguresis during periods of penicillin therapy has been suggested.<sup>82</sup> Colloidal penicillin, formed by the combination of crystalline penicillin with human plasma protein to make a large penicillin-protein complex, is apparently more slowly absorbed from the injected muscle and more slowly excreted by the kidneys than is free or unbound penicillin.<sup>83</sup> This work was done with mice, and the therapeutic efficiency in man is now under investigation. The oral administration of benzoic acid, combined with restriction of caloric intake, fluids and salt, has been found to increase the penicillin blood level, with a prolonged effective blood concentration following intramuscular injection of the drug.<sup>84</sup>

Of these numerous methods of prolonging the action of penicillin, several hold much promise. It is to be hoped that a practical and effective plan will be worked out in the near future so that more efficient use can be made of this remarkable agent.

#### *Oral Administration*

A considerable number of papers concerning the use of penicillin by mouth have appeared. Simplified methods of administering the drug that will provide adequate and prolonged blood concentrations are being sought by many investigators,<sup>85-90</sup> and it is natural that oral administration should be attempted. The destructive action on penicillin by the hydrochloric acid in the stomach can be eliminated by the use of the buffer action of trisodium citrate, disodium phosphate or sodium bicarbonate. The stabilizing effect of protein is also useful, such as penicillin mixed with raw egg. Enteric-coated penicillin tablets gave unsatisfactory results, but penicillin in an oil or fat suspension has proved therapeutically effective. Cottonseed oil, corn oil, peanut oil and beeswax have been used. A method of oral administration of penicillin modified with aluminum hydroxide or magnesium hydroxide has been found effective.<sup>91</sup> Because of prolonged penicillin concentrations in the blood following this method of oral administration, it may have some prophylactic value.

The advantages of giving penicillin by mouth include ease of administration and avoidance of hospitalization, with its attendant economic burden. Relatively crude or impure penicillin would presumably be satisfactory. Therapeutically effective blood levels can be maintained by several of the

tions that they are not solely responsible for post-arsphenamine jaundice. During both world wars a definite relation between the increased incidence of jaundice in the general population and the increased number of cases of post-arsphenamine jaundice was observed. Although an analysis of 119 cases suggested that there was some relation between infective jaundice and post-arsphenamine jaundice, this could not be proved. An attack of late post-arsphenamine jaundice presumably confers no immunity against infective jaundice. Evidence that an attack of infective jaundice also confers no immunity against post-arsphenamine jaundice is incomplete but suggestive.

A case of jaundice following the injection of Mapharsen exhibited clinical and laboratory data consistent with the diagnosis of extrahepatic biliary obstruction.<sup>60</sup> This was not confirmed at operation, and biopsy of the liver showed that the jaundice was intrahepatic. During the course of the disease, the patient developed a syndrome that resembled sprue in many respects. This is unusual.

There has been considerable difference of opinion in the past regarding continuance of antisyphilitic therapy after the development of jaundice. It is generally agreed that arsenotherapy must be stopped for a period of at least several months, but some investigators have concluded that it is safe to continue bismuth. Forbes<sup>61</sup> compared two groups of patients with post-arsphenamine jaundice, one of which was continued on intramuscular injections of bismuth and the other of which received no further antisyphilitic treatment. Clinically, there was no significant difference in the progress of the two groups. The results of liver-function tests indicated that bismuth therapy did not significantly retard recovery of liver function in the treated cases. Such a result supports the view that bismuth therapy may be continued in the presence of jaundice of this nature.

### *Blood Dyscrasias*

In general, Mapharsen has produced fewer reactions than has any of its predecessors. A number of reports have appeared during the past year, however, regarding damage to blood-forming organs from the use of this drug. Agranulocytosis is recorded in 5 cases and from three different sources.<sup>62-64</sup> Aplastic anemia, acute agranulocytosis and thrombopenic purpura are all described as complicating Mapharsen therapy in the same patient.<sup>65</sup> Thrombocytopenic purpura is listed separately.<sup>66</sup>

### *Hemorrhagic Encephalitis*

In addition to the cases already referred to,<sup>53, 55, 56</sup> a discussion of 5 patients with hemorrhagic encephalitis has been published by Lydon.<sup>67</sup> These cases comprise 9 per cent of 53 treated for early syphilis by an intensive course of multiple injections of Mapharsen. The author gives a detailed descrip-

tion of their courses. He believes that alcoholism may be a predisposing factor, as may also a deficiency of vitamin B<sub>1</sub>. Microscopic changes in the liver found at autopsy supported the latter concept. It is suggested that primary cellular damage of the brain tissue itself is a likelier pathologic development than that predicated by the more usually accepted vascular toxic theory. In addition to the customary treatment of venesection, repeated lumbar punctures and adrenalin, the author suggests vitamin B<sub>1</sub> as both a prophylactic and a therapeutic agent. He also used calcium gluconate as an adjunct.

### PENICILLIN

From the information so far available, penicillin seems to be a therapeutic agent of immeasurable value for the treatment of syphilis, with the reservation that the optimal dosage and time-dose relation is not yet fully understood. Emphasis should again be laid on the time required to assay the value of any treatment in syphilis. It will probably be not less than twenty years before the final results of penicillin therapy can be evaluated. Some observers believe that this drug should not be used in the treatment of syphilis outside of research institutions. Nelson<sup>68</sup> states that it should not be employed in private practice or as routine therapy anywhere unless adequate follow-up facilities are available. He goes on to point out that it is not yet certain that the penicillin itself is the effective agent, since the alleged impurities present in commercial preparations may possibly be of greater value than the penicillin. Moore<sup>69</sup> thinks that there is still much to be learned regarding dosage.

It is generally agreed that a total dosage less than 1,200,000 units is followed by an extremely high relapse rate, even with this amount, a relapse rate of 15 to 20 per cent is experienced in early syphilis. It is known that intramuscular injections at three-hour intervals day and night are required. Increasing the amount of penicillin given at three-hourly intervals to reduce the duration of treatment is not helpful. It is known that penicillin is apparently effective in cases of early syphilis that are resistant to arsenic and bismuth. There is some evidence that penicillin in combination with an arsenoxide is more effective than either drug alone. A number of dose schedules are under trial in various treatment centers. Reactions from penicillin have so far been negligible except for the Jarisch-Herxheimer reaction. The present minimum requirement of ten days' hospitalization imposes such an economic burden as to preclude the use of penicillin in many cases. Much work is being done to establish a method for use in ambulatory patients.

Further evidence of the lack of knowledge of this subject can be found in the latest publication of indications and dosage schedules for certifiable penicillin products.<sup>69</sup> It is stated therein that

syphilis is a disease in which penicillin has been found to be an effective agent, but that its position has not been definitely defined and will require additional experimental work

#### *Effect on Treponema pallidum*

It has been demonstrated that *Treponema pallidum* can become resistant to penicillin<sup>70</sup> The work was done with experimental infection of rabbits, which were given sufficient penicillin to modify the course of the disease but not enough to effect a cure This resulted in the development of a penicillin-fast strain, which persisted after further animal passages This emphasizes the necessity for adequate treatment with penicillin in clinical cases It has further been shown that although a single dose of penicillin may sterilize an infectious lesion, even an extremely high single dose is not sufficient to cure experimental syphilis in rabbits<sup>71</sup> This is a good example of the importance of the time-dose relation

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above methods of administration, but the dosage must be markedly increased, as much as five times the intramuscular dose has been found necessary when the drug is given by mouth. Penicillin has also been administered by rectal suppository.<sup>92</sup>

### *Penicillin in Early Syphilis*

Various schedules of treatment were assigned by the Penicillin Panel of the Subcommittee on Venereal Diseases, Division of Medical Sciences, National Research Council.<sup>93</sup> It was quickly found that doses smaller than 1,200,000 units were entirely unsatisfactory, either alone or combined with arsenotherapy. Although lesions healed rapidly and positive dark-field examinations became negative, relapse was the rule. This emphasizes the importance of careful scrutiny for hidden early syphilis in all patients with gonorrhea treated with penicillin. Cases of secondary syphilis developing in such patients still continue to be reported from time to time.<sup>94, 95</sup> The appearance of syphilis is merely delayed by the doses used for gonorrhea.

The time-dose relations of penicillin therapy probably require more study than does any other phase of this treatment problem. A trial of ten different regimens has been reported by McDermott, Benoit and DuBois.<sup>96</sup> Their observations suggested that only short periods of penicillin action are necessary for the immediate destruction of large numbers of the organisms, but that prolonged penicillin action is necessary for cure. Analysis of the various treatment programs under investigation showed that the frequency and size of the separate doses determined the total period of time during which effective concentrations of penicillin were present in the serum. It is apparently not the production of multiple peaks of high concentrations of penicillin but the length of the action at low concentrations that is the important factor. The maximum number of hours of efficient blood-level concentration appears to be obtained by a dosage of 25,000 units intramuscularly every two hours for ten days. It is to be hoped that some of the means of prolonging the action of the drug be discovered whereby a dosage schedule of one or two injections daily will produce satisfactory blood levels for the entire twenty-four hours.

The final evaluation of the ideal penicillin dosage for the treatment of early syphilis must await a prolonged period of study. Obviously, it is impossible to prove at this time that the penicillin programs suggested are superior to those already under investigation. Since, however, it appears that the length of time of penicillin action is the most important factor in the success of a given regimen, it is possible that a consideration of this time factor would help to limit the number of plans for study to those with the most promise.

Although arbitrary schedules at first suggested that a dosage of 1,200,000 units of penicillin was

satisfactory for the treatment of early syphilis, evidence is accumulating that much more than this may be necessary.<sup>68, 97</sup> The total dosage recommended for treatment of early syphilis in the United States Army<sup>98</sup> over a year ago was 2,400,000 units. The Navy<sup>99</sup> recommends a similar dosage in seven and a half days. Even with this amount, some observers<sup>100</sup> have noted a lower percentage of cures than might have been expected.

Early syphilis resistant to arsenic and bismuth has been found to respond satisfactorily to penicillin. A group of 6 cases of the notoriously resistant psoriasiform secondary syphilis was shown to respond to varying doses of penicillin.<sup>101</sup> Some patients required more than one course of penicillin. There is another case on record in which the patient still had dark-field-positive lesions after two and a half years of standard chemotherapy (irregularly administered).<sup>102</sup> Ten weeks of combined bismuth and arsenotherapy then failed. Complete healing was obtained nineteen days after the injection of 1,200,000 units of penicillin within a period of four days.

### *Penicillin in Late Syphilis*

The individualization that the treatment of late syphilis requires makes statistical evaluation extremely difficult. Material from the University of Pennsylvania<sup>103</sup> graphically illustrates that penicillin alone in the management of late syphilis, although of tremendous import, is probably not the ultimate answer. The combination of penicillin with arsenic and with fever therapy may well be of still greater value. The data indicate clearly that penicillin is an effective therapeutic agent in the treatment of late syphilis. Doses seldom exceeded 2,400,000 units, although some cases required re-treatment.

The United States Navy<sup>99</sup> dosage for latent syphilis is 4,000,000 units in twelve and a half days.

### *Congenital Syphilis*

A preliminary report of the results of penicillin therapy in the treatment of 69 infants with early congenital syphilis showed in general a gratifying immediate response.<sup>104</sup> The dosage used consisted of 16,000 to 32,000 units of penicillin per kilogram of body weight, given in sixty doses over a period of seven and a half days. Five patients died during or soon after treatment, but whether these deaths were due to penicillin or to syphilis is not known. Serologic relapse occurred in 5 cases, and clinical relapse in 2. The results indicate that the present schedules are not entirely satisfactory with respect either to the total dose or to the time-dose relation. The authors recommend temporarily a total dose of 40,000 units per kilogram of body weight. More encouraging results have also been reported.<sup>100</sup>

### *Neurosyphilis*

There is disagreement as to the amount of peni-

cillin that will reach the cerebrospinal fluid after administration by parenteral routes<sup>105 106</sup> Nevertheless, its effectiveness in various types of neurosyphilis seems established

Nelson and Duncan<sup>107</sup> treated 10 patients with acute syphilitic meningitis with penicillin Four million units was given over a period of seven and a half to eleven days, and the immediate results were excellent from both clinical and laboratory standpoints There was no evidence of clinical relapse in any patient, although one showed relapse in the spinal-fluid findings after six months Intrathecal administration was found unnecessary

The University of Pennsylvania group<sup>108</sup> found that practically all forms of neurosyphilis showed an encouraging response to penicillin therapy A subsequent report on 89 of their cases stated that improvement in the blood serologic reactions in neurosyphilis and an even greater effect on the elements of the spinal fluid apparently continued for as long as four months after an eight-day course of treatment<sup>109</sup> Both the dosage and the length of treatment were found important in the results The responses were obtained when the length of treatment was increased Better ones were obtained from high doses than from low, — 4,000,000 units against 1,200,000 units, — and the best result followed a high dose given in two parts Rose<sup>109</sup> combined intramuscular penicillin with fever therapy and reported encouraging results A smaller group of patients was treated by Goldman<sup>110</sup> with a combination of spinal and intramuscular penicillin or fever therapy and intramuscular penicillin, the early results were extremely favorable The spinal nerve-root pains of tabes dorsalis were apparently rapidly relieved by the intraspinal administration of penicillin Further work with the subarachnoid administration of penicillin indicates that this method entails considerable danger but holds promise<sup>111, 112</sup>

The present routine of treatment employed in the Navy<sup>99</sup> involves the administration of 8,000,000 units of penicillin in twenty-five days for the treatment of syphilis of the central nervous system, followed by ten courses of artificial fever accompanied by ten intravenous injections of penicillin, each of 60,000 units

It has been found that penicillin does not suppress the fever or parasite count of active inoculated malaria, and that when given before or at the time of the malaria inoculation it does not prevent or postpone the development of fever and parasitemia<sup>113</sup> Obviously, there should therefore be no contraindication to the use of penicillin before, during or after malaria

#### *Penicillin Reactions*

Penicillin reactions in the treatment of syphilis, although minor, are not negligible The Herxheimer reaction may occur, and in cases of late syphilis

such a focal reaction in a vital structure may be grave Consequently, half the customary dose on the first day or even the second day may be advisable in many cases This reduction should be compensated by a prolongation of the course

Urticaria,<sup>114</sup> some transient gastrointestinal reactions and exfoliative dermatitis<sup>115</sup> have been observed in patients previously intolerant to treatment

Contact dermatitis from penicillin has been reported a number of times<sup>114-116</sup> In one case,<sup>117</sup> it could be proved that impurities were the offending agent The possibility of penicillin in the role of a future sensitizing agent has also arisen<sup>118</sup>

#### SUMMARY

Approximately 25 per cent less cases of syphilis of all varieties were reported in this country during the first half of the fiscal year of the United States Public Health Service It is to be hoped that this means a lowered incidence as well as a more effective campaign for the control of this disease The first mass civilian blood-testing program has been started in Alabama This is the result of a law passed by the state legislature and will be of tremendous import if pursued on a nation-wide scale It could easily be the one most important control measure ever employed The value of educational programs for the general public is proving itself The staggering burden of syphilis on the taxpayer is illustrated by the fact that the care of general paresis alone costs over \$11,000,000 annually, aside from the economic loss to the patients afflicted

The problem of false-positive tests for syphilis continues to receive a great deal of attention The effectiveness of rapid-treatment programs and of penicillin in the therapy of syphilis has made the problem of relapse versus reinfection an extremely intricate one It seems generally agreed that all such cases should be considered treatment failures when assaying the value of new treatment programs

More attention has apparently been directed in recent clinical reports toward neurosyphilis than to any other phase of the disease Considerable new statistical data and several excellent reviews of neurosyphilis in all its varieties are available Intensive-treatment schedules show encouraging results in neurosyphilis, although the time of observation for these patients is not long enough The first survey of massive arsenotherapy on a comprehensive scale indicates that the good results reported earlier have been maintained Hemorrhagic encephalitis continues to be a most disturbing complication More reactions are being observed from the use of Mapharsen, especially blood dyscrasias

Penicillin is assuming an ever greater importance in the treatment of syphilis Investigative studies are mushrooming in all directions in attempts to increase the effectiveness and to prolong the action time of this drug Some investigators have raised the question whether pure penicillin itself is the ac-

tive agent in the treatment of syphilis. Resistant strains of *Treponema pallidum* have been developed experimentally. Much work has been done with the oral administration of penicillin with encouraging results. So long as hospitalization is required, with its attendant cost and increased burden on hospital facilities, the use of this drug will be somewhat limited. The optimal dose of penicillin in the treatment of syphilis is yet to be determined, and the time-dose relation is not properly understood. Present indications are that more prolonged administration will be necessary. The combination of penicillin with arsenotherapy has been producing most promising results. Reactions to penicillin continue to be comparatively insignificant.

As a brief statement of the situation, it may be said that penicillin is as yet incompletely analyzed and poorly understood. It seems to be an effective therapeutic agent in the treatment of syphilis, with less reaction than is caused by any previous drug. It cannot be too strongly emphasized that penicillin must continue to be regarded as purely an experimental drug in the treatment of syphilis, and that a minimum of ten to twenty years must elapse before its true value can be accurately assayed. Every serious investigator has stressed this point, and editorial comment has repeatedly emphasized it. One might say that patients treated with penicillin should be followed much more closely and over a greater period of years than ever before. It is to be hoped that military personnel will be included in this careful follow-up program.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 32111

#### PRESENTATION OF CASE

A nine-year-old Negro girl was admitted to the hospital because of cervical and axillary lymphadenopathy.

The patient had had no chills, night sweats, joint pain, nocturia, anorexia or upper respiratory infection. The swelling of the lymph nodes had been noted four weeks before entry. She had not seemed ill and had gained weight during the month previous to admission. The teeth were in poor condition and had caused some pain for a three-week period before admission. A child with whom the patient had played two weeks before admission had developed swollen lymph nodes and fever, which subsided in one week. The patient developed fever two days before admission.

The past history was negative except for pertussis.

Physical examination revealed a well developed and well nourished, co-operative child, who did not appear ill. The skin was hot and dry. The cervical, posterior auricular, occipital, supraclavicular, epitrochlear, axillary and inguinal lymph nodes were enlarged, soft, nontender, movable and discrete, the nodes averaged 1.5 to 2 cm in diameter, except for the left supraclavicular node, which measured 4 by 3 cm. The pupils, eyegrounds, ears and nose were normal. The pharynx was slightly congested. The tonsils were not markedly enlarged. The teeth were carious. The neck was not stiff. The heart was not enlarged. A soft systolic murmur

was heard in the left third interspace and was not transmitted. The lungs were clear. The edge of the liver was palpable at the right costal margin. The spleen was palpated one fingerbreadth below the left costal margin. The common peroneal reflex and the signs of Chvostek and Trousseau were elicited.

The temperature was 103°F, the pulse 96, and the respirations 22. The blood pressure was 110 systolic, 70 diastolic.

The red-cell count was 4,200,000, with 8.6 gm of hemoglobin. The white-cell count was 22,000, with 83 per cent neutrophils. No malarial parasites were seen on smear. The urine was yellow, slightly cloudy and acid, with a specific gravity of 1.020 and a +++ test for albumin. The urinary sediment contained 8 to 10 white cells, no red cells and a rare cast per high-power field. The nonprotein nitrogen was 21 mg per 100 cc, and the serum protein 7.8 gm, with 3.0 gm of albumin and 4.8 gm of globulin. The serum calcium was 6.2 mg per 100 cc, the phosphorus 3.0 mg, and the alkaline phosphatase 8.4 Bodansky units. The serum sodium was 147.5 milliequiv per liter, the chloride 102 milliequiv, and the carbon dioxide content 27.7 milliequiv. The serum potassium was 4.9 gm per 100 cc, and the cholesterol 114 mg. Tests for heterophile and brucella agglutinins were negative. A tuberculin test was negative in a dilution of 1:1000. The Frei test was negative. The sedimentation rate was 0.9 mm per minute (Rourke-Ernstene method). Soon after admission one blood culture showed alpha-hemolytic streptococci, and another, nonhemolytic streptococci. Several others were negative.

An x-ray film of the chest showed a diffuse increase of all markings throughout both lung fields and a few nodular densities in both hilar shadows, more clearly seen on the right than on the left. An x-ray film of the abdomen showed some enlargement of the spleen, but no enlargement of the liver and no abnormal masses. A film of the skull was negative, and one of the teeth showed marked apical absorption about retained deciduous root fragments in the region of the second right molar area. The skeleton was not remarkable. An intravenous pyelogram revealed that the right kidney was normal.

tive agent in the treatment of syphilis. Resistant strains of *Treponema pallidum* have been developed experimentally. Much work has been done with the oral administration of penicillin with encouraging results. So long as hospitalization is required, with its attendant cost and increased burden on hospital facilities, the use of this drug will be somewhat limited. The optimal dose of penicillin in the treatment of syphilis is yet to be determined, and the time-dose relation is not properly understood. Present indications are that more prolonged administration will be necessary. The combination of penicillin with arsenotherapy has been producing most promising results. Reactions to penicillin continue to be comparatively insignificant.

As a brief statement of the situation, it may be said that penicillin is as yet incompletely analyzed and poorly understood. It seems to be an effective therapeutic agent in the treatment of syphilis, with less reaction than is caused by any previous drug. It cannot be too strongly emphasized that penicillin must continue to be regarded as purely an experimental drug in the treatment of syphilis, and that a minimum of ten to twenty years must elapse before its true value can be accurately assayed. Every serious investigator has stressed this point, and editorial comment has repeatedly emphasized it. One might say that patients treated with penicillin should be followed much more closely and over a greater period of years than ever before. It is to be hoped that military personnel will be included in this careful follow-up program.

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of miliary tuberculosis. I believe much of the information recorded must have been obtained by fluoroscopy since I cannot see much of anything in these two films. The films do not suggest a pericardial effusion, but I suppose that that is a possibility. There is dullness anterior to the heart in the lateral view, suggesting a mediastinal mass.

DR KLEMPERER: What do you think this mass is?

DR HOLMES: It could be a mediastinal tumor—a Hodgkin's type of lymphoma or a large thymoma.

DR KLEMPERER: This comes as a surprise. Nevertheless, these x-ray films rule out miliary tuberculosis.

In regard to infection, subacute bacterial endocarditis is suggested by the two positive blood cultures, possibly by the diastolic murmur, which was heard at one time and by the enlargement of the spleen. If this child's death had been due to subacute bacterial endocarditis, however, I should have expected more evidence of a progressive valvular lesion and probably embolic phenomena. The kidney lesion does not resemble the embolic nephritis seen in subacute bacterial endocarditis. Because the hematuria was preceded by albuminuria, subacute bacterial endocarditis might have been present, but I do not believe that it was the primary cause of this child's illness. After ruling out infection as the primary disease we must consider a group of diseases that, so far as we know, are not infectious in origin but are capable of involving various systems of the body. Among these the likeliest are lymphoma, sarcoid and possibly periarteritis nodosa and disseminated lupus erythematosus.

Hodgkin's disease is strongly suggested by the onset with adenopathy. We do not know about any constitutional symptoms that might have preceded the appearance of the enlarged lymph nodes. It is also suggested by the size and the distribution of the lymph nodes. Hodgkin's disease may be acute and lead to death in a single attack, with high fever. What bothers me about Hodgkin's disease in this patient is first, the kind of renal involvement. I have never seen or heard of a patient with lymphoma in whom albuminuria and subsequent hematuria were the outstanding symptoms and signs and whose death was caused by renal failure. The next point that I believe almost rules out this diagnosis is that the biopsy did not show any specific lesion. The surgeon must have removed an obviously enlarged node, and if it was Hodgkin's disease it should have been demonstrated in the excised specimen.

DR HOLMES: I hope that I have not been misleading you. As I look through the record I find that a film taken at one time showed an apparently normal-sized heart shadow. That makes my interpretation of tumor most unlikely. A tumor would not appear in such a short period of time. In other words, the mass probably represents an enlargement of the heart shadow.

DR KLEMPERER: I shall also consider lymphoma unlikely for the reasons stated.

I then come to sarcoid. This is suggested by the symptoms and by the lymphadenopathy that initiated the illness. We know that sarcoid can involve every organ in the body. Cardiac involvement, pulmonary involvement and, quite frequently, renal involvement are known to occur. I have not seen nor to my knowledge has a case been reported in which renal involvement dominated the picture. The main reason why I want to throw out sarcoid is that the patient was much too sick. Sarcoid usually runs a long course and seldom causes a white-cell count as high as this was. Furthermore, one of the arguments that I used against Hodgkin's disease or lymphoma in general may be applied against the diagnosis of sarcoid, namely, that the biopsy was negative.

Periarteritis nodosa is the next consideration. I should like to think of this lesion as a more or less nonspecific tissue reaction that is not necessarily a disease entity. Dr Francis M. Rackemann frequently stresses this point. Such a tissue reaction is seen in various stages of sensitivity and may also be seen in disseminated lupus. It should be called a disease entity only in the presence of a clear-cut clinical picture. In the absence of asthma, joint pains and eosinophilia, this diagnosis seems untenable. The renal involvement is not characteristic, and I am at a loss to explain the adenopathy on the basis of periarteritis nodosa. I shall rule it out.

That leaves me with lupus erythematosus as a final possibility. There are several factors against it. Lupus erythematosus usually affects young adults, although it is known that it rarely occurs in children. We have seen it in a girl before the onset of menstruation, and similar cases have been described in the literature. The age, therefore, does not permit me to rule out lupus. The patient had a white-cell count of 22,000. One frequently hears the statement that lupus should always be accompanied by leukopenia. That is not true. Frequently the white-cell count is below 5000, but I have seen several cases with a white-cell count as high as this, and a number of cases are cited in the literature. The onset of the disease is likewise quite atypical. Usually the initial symptoms in lupus are skin rash, joint pains and constitutional symptoms. I have not seen or heard of a case of lupus that started with adenopathy, but I question the history. I wonder if the patient might have run a fever long before she came to the hospital. On admission she had renal involvement with a low calcium and tetany that must have existed for some time, and yet she had no complaints. I wonder if they were missed. Adenopathy is quite frequent in lupus, about half the cases show it, at times to a fairly marked degree. The renal involvement in this patient is quite characteristic, beginning with

in size, shape and position. The left kidney was not well visualized at any time. The intravenous dye appeared promptly in good concentration, outlining normal urinary passages.

During the patient's hospital course the temperature varied from 98 to 106°F, usually running between 100 and 102°. Soon after admission a lumbar puncture showed clear fluid under an initial pressure equivalent to 300 mm of water, the cell count and chemical constituents were normal. The patient was given sulfadiazine, 5 gm every four hours, and penicillin, 12,000 units every three hours. On the third hospital day, since the blood sulfadiazine level had risen to 74 mg per 100 cc and sulfadiazine crystals had appeared in the urine, the drug was discontinued. A lymph-node biopsy showed hyperplasia. Albuminuria persisted, with 10 to 15 white cells, numerous red cells and many hyaline, granular and red-cell casts per high-power field. On the twelfth hospital day a chest film showed enlargement of the heart to the left and right, with pulmonary edema. On physical examination there were no rales. The pulse rate was 120, the blood pressure was 128 systolic, 76 diastolic. The heart sounds were of poor quality. There was a gallop rhythm, with short diastole, and a soft mid-diastolic murmur at the mitral area. The liver was enlarged three fingerbreadths below the right costal margin. The abdomen was doughy and distended, apparently containing a small amount of fluid. An electrocardiogram on the same day showed normal rhythm, with a rate of 110. There was slight right-axis deviation. The PR interval was 0.12 second. There was slight inversion of T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub> were upright, TCF<sub>2</sub> was moderately inverted, TCF<sub>4</sub> was inverted, and TCF<sub>5</sub> was flat. The patient was rapidly digitalized, and the heart sounds improved. The blood pressure was 110 systolic, 50 diastolic. The nonprotein nitrogen was 31 mg per 100 cc, the serum phosphorus 4.1 mg, the alkaline phosphatase 2.3 Bodansky units, and the serum protein 8.1 gm per 100 cc.

A chest film taken on the seventeenth hospital day revealed marked enlargement of the heart, which showed small, rapid, but definitely perceptible pulsations. The pulmonary and hilar vessels were considerably engorged. There was a definite, small area of localized density in the right chest laterally, above the diaphragm. There was also hazy increased density throughout both lungs. The patient was drowsy and irritable. There was no dyspnea or orthopnea. The heart sounds were forceful and rather metallic in character. There was a precordial systolic murmur. The lungs were dull at the bases, without rales. The abdomen was distended. The liver edge was tender and 4 cm below the right costal margin in the midclavicular line. The spleen was palpable 2 cm below the left costal margin. There was no edema of the sacrum or legs. The eyelids were slightly puffy. There was

no skin rash. At that time the urine was smoky and alkaline, had a specific gravity of 1.020 and gave a ++++ test for albumin. The sediment contained 20 to 30 white cells, numerous red cells and frequent granular casts per high-power field. The eyegrounds for the first time showed hyperemic choked disks, more marked on the right than on the left. There was no retinal hemorrhage or scarring.

A chest film taken on the twenty-second hospital day showed no change in the size of the heart but some decrease in the engorgement of the hilar and pulmonary vessels. The nonprotein nitrogen was 29 mg per 100 cc, the serum protein 7.0 gm, the cholesterol 147 mg, and the potassium 5.2 miliequiv per liter. The prothrombin time was 26 seconds (normal, 18 seconds).

Penicillin was discontinued on the thirty-third hospital day. The abdomen became markedly distended, and generalized pitting edema appeared. The blood pressure was 82 systolic, 35 diastolic. The heart sounds were of poor quality. Slow epistaxis occurred. The respirations were shallow, and the diaphragm was high. The breath sounds were coarse, especially at the bases, but there were no rales. The nonprotein nitrogen rose to 70 mg per 100 cc.

On the thirty-sixth hospital day the respirations became more rapid. The pulse was full and strong but paradoxical. The patient was put in an oxygen tent and was reasonably comfortable lying flat. Venous distention was not marked. Edema of the legs increased. Rales appeared at the lung bases for the first time. Dyspnea and a hacking cough were troublesome. After a period of irregular respirations the patient expired, on the thirty-ninth day.

#### DIFFERENTIAL DIAGNOSIS

DR FRIEDRICH W KLEMPERER. In summary, we are dealing with a nine-year-old colored girl who, within five weeks, developed adenopathy, renal involvement, cardiac involvement and probably pulmonary involvement and died. This course suggests infection, but such diseases as infectious mononucleosis, brucellosis or lymphogranuloma inguinale were ruled out by the serologic and skin tests. I see no mention of a Hinton test, but aside from the adenopathy, which in this case would not be characteristic, I see nothing to suggest syphilis. There was a negative tuberculin test. This does not rule out tuberculosis because in miliary and rapidly progressing tuberculosis the tuberculin test may be negative. I do not believe, however, that this was tuberculosis, particularly because of the character and distribution of the lymphadenopathy, which was not suggestive of this disease. If this had been miliary tuberculosis I should have expected a different description of the x-ray films.

I should like to see the x-ray films. Is there anything to suggest a miliary process in the lungs?

DR GEORGE W HOLMES. There is no evidence



cavity. For a girl as small as this patient was, that is significant effusion. Since the fluid was perfectly clear, with no strands of fibrin, it cannot be said that she had a pericarditis. The heart weighed 155 gm, perhaps slightly enlarged. The pair of kidneys, in contrast, weighed 300 gm, in other words, there was marked enlargement. The kidneys microscopically showed a diffuse glomerulonephritis, with both intracapillary and capsular changes, including many epithelial crescents. There were secondary although still fairly early degenerative changes in the tubules. We saw nothing in the kidneys to suggest sulfonamide damage. The lymph nodes at autopsy showed nothing more spectacular than the one that was biopsied. The thymus was extremely large, weighing 50 gm, which is nearly twice the normal size for a child of this age, and perhaps that is what Dr Holmes pointed out.

Our anatomical diagnosis was subacute glomerulonephritis, and we have no explanation for the enlarged lymph nodes. We found none of the usual findings at autopsy that would help to confirm a diagnosis of lupus erythematosus. The lymph-node picture in that disease is not specific, but there are likely to be a number of rather characteristic changes, which were not present here. She had effusions in various serous cavities but no inflammatory changes in any of them. A diffuse glomerulonephritis is occasionally seen in characteristic cases of lupus, but it is not the usual lesion; ordinarily one finds either focal glomerulonephritis or the so-called "wire-loop" lesion described by Baehr, Klemperer and Schiffin\*. I can neither confirm nor disprove the diagnosis of lupus erythematosus. It remains a possibility. Certainly, the anatomical diagnosis of subacute glomerulonephritis does not explain a great deal of the picture.

## CASE 32112

### PRESENTATION OF CASE

A forty-six-year-old woman, a spinner in a textile mill, was admitted to the hospital for pain in the right chest.

Three years prior to admission the patient developed an annoying and slightly painful sensation in the right posterior axillary line overlying the tenth and eleventh ribs. She likened the sensation to "numerous mosquito bites." Her physician performed several thoracenteses, with negative results. No x-ray studies were done. The episode subsided after three weeks and did not recur. Two years later, one year before admission, a routine chest film taken at the mill where she was employed was reported as normal. At about that time she began to have attacks of moderately severe pain

in the same previously affected area of the right chest. The pain was steady, aggravated by inspiration and partially relieved by lying down. She had frequently been awakened by it but had never had to take medicine for relief. Each attack lasted from one to three weeks. At first they occurred every two to three months, but as the year progressed the intervals between attacks were gradually lessened until the pain was almost constant. There had been no cough, sputum, hemoptysis, night sweats or known exposure to tuberculosis. She had lost 6 pounds in the six months prior to admission. One month before admission her physician obtained a chest film, which was reported to have shown a "large spot in the middle lobe."

At the age of eight years a mass in the left submandibular region ruptured and drained spontaneously; there were no sequelae.

On physical examination there was slightly increased vocal fremitus over the right upper chest and questionable increased whispered voice sounds in the same area. Tactile fremitus was normal, as were percussion and auscultation. There was a well healed scar 5 cm long over the left submandibular region.

The temperature was 98°F, the pulse 85, and the respirations 20. The blood pressure was 145 systolic, 95 diastolic.

The red-cell count was 4,250,000, with 13 gm of hemoglobin. The white-cell count was 11,200, with 82 per cent neutrophils, 14 per cent lymphocytes and 4 per cent monocytes. The urine was normal. The serum protein was 6.2 gm per 100 cc. An x-ray film of the chest revealed an area of increased density, with superimposed linear areas of greater density, in the posterolateral portion of the right lower lobe. The right hilus was somewhat depressed. The remaining lung fields appeared clear. The diaphragm moved freely and equally. The costophrenic sinuses were flattened. The heart, aorta and upper mediastinum were within normal limits (Fig 1).

On the second day after admission bronchoscopy was performed. Just beyond the upper lobe opening, the lumen of the right bronchus was markedly narrowed by a concentric constriction. No tumor mass was seen. The mucous membrane was normal. The bronchoscope could not be passed below this level. Smooth forceps were passed beyond, but no palpable outcropping was encountered.

An operation was performed on the seventh hospital day.

### DIFFERENTIAL DIAGNOSIS

DR MILES P. BAKER. The chief considerations in this case seem to be the etiology of the constriction found in the right main bronchus and the nature of the process demonstrated by x-ray in the right lower lobe. I think that I had better ask to see the films now.

\*Baehr G., Klemperer P. and Schiffin A. Diffuse disease of peripheral circulation usually associated with lupus erythematosus and endocarditis. *Tr. A. M. Physicians* 1:139-155, 1935.



albuminuria and leading to hematuria and eventual renal failure

Cardiac failure can take several forms in lupus erythematosus. The picture given here is quite consistent with that diagnosis. One naturally thinks of pericarditis. It is stated in the record that by fluoroscopy there were definite pulsations but that they were weak. The electrocardiographic changes may be explained on the basis of pericarditis or myocardial involvement, but toward the end there was a paradoxical pulse, and if this observation was correct, it is strongly in favor of a diagnosis of lupus erythematosus, which so frequently is complicated by serositis. The involvement of the heart might have been on the basis of the diffuse myocardial involvement that is occasionally seen in lupus. A mid-diastolic murmur was heard at one time, but a later report says that a systolic murmur was heard, which means to me that only a systolic murmur was heard, so we are not certain whether the patient had mitral involvement. If the patient did have mitral involvement, I should interpret it on the basis of Libman-Sacks endocarditis. We know that this endocarditis is frequently complicated by bacterial invasion, which may have been the case in this patient, who showed positive blood cultures on two occasions.

Whether there was involvement of the lungs, I am not quite certain from the clinical record. One quite frequently sees a picture that resembles a shifting bronchopneumonia in lupus, and some of the x-ray findings, that is, the increased density, may be explained on that basis.

I believe that the abnormalities of the blood constituents are explained on the basis of the renal lesion, particularly the low calcium, which led to tetany. A high globulin is not infrequent in lupus, and in some series it has been found almost in all cases. We have seen it in some.

In reading this record one gets the impression that the child was not particularly ill when she came to the hospital, but from the time that she was given sulfonamides, her disease rapidly progressed to death. I do not know why the child was given sulfonamides. So long as a diagnosis of lupus is a possibility, I think that sulfonamides should be withheld, because in our experience the administration of sulfonamides in patients with lupus has produced severe exacerbations. So, this exacerbation following the administration of sulfonamides may also be interpreted in favor of the diagnosis of lupus. Although I believe that the child's age and the absence of skin lesions and joint pains argue somewhat against the diagnosis of lupus erythematosus, I can think of no other disease entity that fits this picture better, and I shall therefore offer it as my diagnosis.

DR TRACY B MALLORY Are there any comments from the Pediatric Service?

DR JOHN D CRAWFORD My first comment is

that the history is accurate. It was rechecked several times, and on several occasions I talked to the patient's mother, who is a very intelligent person.

The patient was first seen in the Surgical Service of the Out Patient Department because of large nodes in the neck, from there she was referred to the X-ray Department, and she finally came to us by way of the Emergency Ward. We did not consider that she was seriously sick on admission, but during the first forty-eight hours in the hospital she ran a spiking temperature, which reached 106°F on two occasions. It was decided, more or less in desperation, to use sulfonamides and penicillin, since the predominance of polymorphonuclear leukocytes in the blood smear suggested an infection. We were not happy about the use of sulfonamides in a patient whose etiologic diagnosis was not established.

Another point that I want to make concerns this child's x-ray studies. The first film, taken when she was seen in the Surgical Service of the Out Patient Department, showed a normal heart with enlarged nodes. The second film, taken four days later when she was admitted to the ward, still did not show an enlarged heart. About ten days after that one of the house officers thought that he heard a murmur, and recommended another x-ray film of the chest. She was sent to the X-ray Department and they reported that the child had acute cardiac failure and pulmonary edema. A greatly enlarged cardiac shadow with pulmonary congestion persisted, despite therapy, from that time until death. We suspected pericarditis in addition, but we thought, since the pulsations showed through every time she was fluoroscoped and since clinically there was no cardiac embarrassment, that the effusion was not great in amount.

#### CLINICAL DIAGNOSES

Acute nephritis  
Myocarditis  
Pericardial effusion

#### DR KLEMPERER'S DIAGNOSIS

Lupus erythematosus disseminatus

#### ANATOMICAL DIAGNOSES

Subacute glomerulonephritis  
Pulmonary congestion and edema  
Anasarca  
Lymphoid hyperplasia, generalized  
Hyperplasia of thymus

#### PATHOLOGICAL DISCUSSION

DR MALLORY Dr Klemperer has shown the discretion to pick a diagnosis that I cannot refute. The significant autopsy findings were the generalized lymph-node enlargement noted clinically and the generalized edema, with about 1000 cc of fluid in the peritoneal cavity and 80 cc in the pericardial

chus One of the causes of bronchostenosis of a fibrostenotic type is, as you know, syphilis. It is of uncommon occurrence and has become even less frequent as gummas and tertiary syphilis are less often seen. I have never seen a proved case. I am told that syphilis of the tracheobronchial tree is likelier to involve the trachea and its bifurcation than the main bronchus, as here. It may produce a constricting obstruction, such as this, but we have no corroborative evidence for such a diagnosis in this case, and there is no other evidence of tertiary syphilis.

I shall mention briefly two other possibilities that may occur as causes of such stenosis. One is actinomycosis, but this too is likelier to involve the trachea as an obstructive lesion. Rhinoscleroma is another condition mentioned in the books, associated with similar changes in the larynx, forming multiple hard annular lesions and sometimes a funnel-shaped stenosis of the trachea and major bronchi. The peribronchial processes that cause marked stenosis usually involve the small branches of the bronchi, not a major bronchus, such as we have involved here. I believe that we can dismiss them from consideration as we have these rarer causes of bronchostenosis.

We come to tuberculosis as a cause of what the bronchoscopist found in this patient's bronchus. A great deal was learned about tuberculous lesions of the trachea and large bronchi in the years shortly before the war as a result of systematic bronchoscopy in many patients with pulmonary tuberculosis in sanatoriums and elsewhere. These observations have demonstrated that a fibrostenotic obstruction may be the end result of spontaneous healing of a tuberculous bronchitis that originally took the form of an ulcerated granulomatous lesion. It takes a long time for healing to take place and for such a stenosis to develop. This type of stenotic obstruction has been found with minimal or no pulmonary tuberculosis, although it is not apparently a common occurrence, and such patients not infrequently develop frank pulmonary tuberculosis under observation.

The origin of bronchial tuberculosis may be extension from peribronchial caseous tuberculous lymph nodes but is much more frequently the result of extension from primary pulmonary disease, usually in the upper lobe but occasionally in the lower lobe. So, although we may say that this obstruction is compatible in appearance with an old tuberculous etiology, we are drawing a rather long bow in assuming that the stenosis was both of many years' standing, possibly dating from adolescence, and due to involvement of the bronchus by tuberculous infection that developed in a juxtaposed caseous lymph node. This happens in children but is not so likely to be seen in adults. This certainly is not the usual story in cases in which fibrostenotic lesions have been observed by bron-

choscopy. Much oftener than not such patients have x-ray evidence of active pulmonary tuberculosis or at least an arrested pulmonary tuberculous lesion. It may not be too farfetched, however, to assume that we are dealing with an old tuberculous lesion on the basis of symptomatology, because symptoms may not arise in these patients with bronchostenosis until they develop infection distal to the constriction—the old story of bronchial obstruction and damage to bronchi, infection, bronchiectasis, abscess and recurrent pneumonitis, usually in a lower lobe. It is interesting to remember that syphilitic bronchial obstruction in the days when it was more frequently seen and reported did not necessarily give rise to bronchiectasis, even though the degree of constriction was marked and oftener than not bronchiectatic changes were found. Unless there is a wheezy dyspnea, symptoms are likeliest to develop in the presence of such bronchial obstruction only when the patient develops infection distal to the obstruction. That is what I think has probably happened in this woman. That is more probably a cause for her pleuritic pain than an entirely different process, such as a tumor in the right lower lobe, something that we cannot absolutely rule out, but I think that it is less likely than infection.

There is no question about the wisdom of surgery. This woman had an obstructive process in the lower lobe and symptoms referred thereto. I believe that the pathologist may not have found any confirmatory evidence of tuberculosis to account for this bronchostenosis. The shadow that we see by x-ray probably does not represent an abscess, but rather an area of pneumonitis. It is quite likely that distal to such a constriction as this woman had there was more bronchiectasis than one might expect in the absence of fever and cough.

DR DONALD S. KING: It comes down to a matter of x-ray interpretation. I assume that the X-ray Department was not convinced of tumor in this case.

DR SCHULZ: But I do not know how one could be certain that there was not a tumor occluding a small bronchus, behind which the findings seen in the chest film had taken place.

DR KING: It is hard to hitch up tumor with the narrow bronchus.

DR TRACY B. MALLORY: I am sorry that Dr Sweet is not here to discuss this case, because I understand that there was a lively argument whether or not the patient should be submitted to surgery. Perhaps you can tell us about that, Dr Miller.

DR CARROLL C. MILLER: Dr Sweet went into the problem with a strong conviction of the advisability of operation and the likelihood of finding cancer. He believed, as Dr Schulz has intimated, that the x-ray appearance was more like that of carcinoma than of the other conditions that Dr Baker has mentioned. He is in favor of exploratory

DR MILFORD D SCHULZ Here is the area in question I do not believe that I can add anything to the written report The area lies laterally and somewhat posteriorly

DR BAKER Can you exclude pulmonary tuberculosis of the upper lobes?

DR SCHULZ Yes, except for evidence of an old healed primary lesion, which represents something long gone by

DR BAKER And it is not impressive There was no attempt made to determine the possibility of

lower lobe There are also recorded a childhood history of lymphadenitis of tuberculous origin, a constricting lesion in the right bronchus, an x-ray lesion in the right lower lobe, which we can see here in the lateral film, and a moderate degree of polymorphonuclear leukocytosis

The interesting negative facts are absence of cough, of sputum, at least of hemoptysis, of fever and of abnormal physical signs in the chest The last is not too extraordinary in the presence of bronchostenosis Some years ago Dr Frederick



FIGURE 1

obstructive emphysema, that is, no films were taken at expiration?

DR SCHULZ No I assume that the fluoroscopist who examined the chest was not impressed with any such possibility

DR BAKER There are a number of important positive facts in this case The first is the three-year story of pain in the right lower chest, which was first intermittent and then became constant and pleural in nature Presumably the patient presented physical signs three years previously that suggested to the attending physician that there was fluid at the right base These signs may of course have been due to atelectasis of the right

T Lord made the comment that with marked bronchostenosis, if there was a small persisting orifice, there might be a striking paucity of abnormal physical signs Moreover, there is no x-ray evidence of obstructive emphysema or of atelectasis We have no evidence of obstruction by a bronchogenic carcinoma or by a so-called "benign adenoma" of the bronchus, which might have been suspected here, even in the absence of hemoptysis We have no information regarding the skin tuberculin test or the blood Hinton reaction, both of which might have had some significance if negative.

We come then to the differential diagnosis of this concentric obstruction in the right main bron-

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## PENICILLIN TREATMENT OF EMPYEMA

At a meeting of the New York Academy of Medicine in November, 1943, Tillett, Cambier and McCormack<sup>1</sup> reported on the treatment of 8 patients with pneumococcal empyema by repeated thoracenteses with aspirations and intrapleural injections of penicillin. In 7 of these patients the infection was eliminated by local treatment and no surgical drainage was required. The same authors<sup>2</sup> subsequently reported on 13 additional cases of pneumococcal empyema, all of which were successfully treated in a similar manner. In 20 of the 21 cases of pneumococcal empyema, these authors obtained recoveries without evidence of residual chronic infection and without thoracic deformity or detectable reduction in pulmonary function. In

14 of the cases a single series of local injections ranging from one to five doses, usually consisting of 30 000 to 50 000 units each given on alternate days proved successful. In 7 cases relapses of the infection occurred when the initial course of treatment was suspended, but reinstitution of local therapy with penicillin resulted in complete and permanent clearing of the infection in 6 of these cases. The single unsuccessful case was in a child two years old who was operated on after the first course of treatment was followed by a relapse. The general condition of all the patients improved before the exudate cleared. Complete clearing according to x-ray films required from three to nine weeks. The average time between the first and last thoracenteses was twenty-four days. Follow-up studies also revealed a return of the affected side to normal functional state and only a limited degree of pleural thickening remained.

There have been a number of subsequent reports on the use of penicillin in the treatment of pneumococcal and other types of empyema. The results obtained in a small series of cases at the Boston City Hospital, as well as an analysis of the cases collected from the literature will be presented in a forthcoming issue of the *Annals of Internal Medicine*.<sup>3</sup>

The reported cases fall into three general groups. The first consists of 128 cases of empyema that occurred as a complication of wounds and of operations on the lungs and pleura. The results in this group were difficult to evaluate because of the variety of underlying conditions and many complicating factors. Several authors, however, believed that intrapleural penicillin was of great help in the management of these cases and that such treatment obviated the necessity for secondary operations for drainage of the empyema in a number of cases.

The second group comprised 15 cases of putrid empyema. These cases, which are often due to mixed infections and are associated with other infectious processes in the lungs or elsewhere, are known to have a high mortality even under the best surgical management. Anaerobic streptococci and a variety of other organisms, some of which are resistant to penicillin, may be present. The use of intrapleural penicillin in these cases resulted in considerable im-

thoracotomy in cases in which there is so much doubt concerning the diagnosis. In addition to the x-ray appearance I think that the bronchoscopist's description is of importance, because we frequently do see cases of carcinoma in which there is constriction of the bronchus without obvious tumor in the lumen of the bronchial tree.

DR KING: That far away from the lesion?

DR MILLER: Yes. We have seen a process extending along the bronchial tree some distance away from the lesion seen by x-ray.

DR MALLORY: Will you tell us about the operative findings?

DR MILLER: On opening the chest there were no adhesions. There was a moderate-sized tumor, quite a bit larger than what was indicated by the x-ray films, in the lower lobe, involving the middle lobe and extending down the hilus, so that the bronchoscopist's findings were easily explained. There were also enlarged lymph nodes around the hilus. In the anterolateral inferior segment of the lower lobe there was a triangular area of induration that had a grayish color on its surface, with a purplish edge. This resembled an infarct. It was thought advisable to do a pneumonectomy rather than a lower and middle lobe lobectomy.

#### CLINICAL DIAGNOSIS

Carcinoma of lung

#### DR BAKER'S DIAGNOSES

Bronchial obstruction, due to healed tuberculosis of bronchus

Pneumonitis, right lower lobe

#### ANATOMICAL DIAGNOSES

**Adenocarcinoma of lung**, with metastases to hilar lymph nodes

**Pulmonary infarcts**, distal to tumor

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The specimen we received at the laboratory was unusual and aroused our interest since none of us could remember having seen anything quite like it. The primary condition was a carcinoma arising in a relatively small bronchus, growing upward toward the hilus along the bronchi and constricting them by external pressure from outside. There was no outcropping in any of the major bronchi that the bronchoscopist could reach. I doubt that it would have been possible for him to take a biopsy, which would have helped settle the issue.

The unusual feature from our point of view was the presence of two foci of markedly increased density in the peripheral portions of the lower lobe. These were in contact with the pleural surfaces and were grossly and microscopically characteristic of old infarcts. It is, of course, of common occurrence to find bronchiectasis and various types of obstructive pneumonitis behind constricted bronchi, but one does not expect to find infarction. We believe that this was explained by the constrictive action of the tumor, which gradually surrounded the major vessels leading to the lower lobe and cut down the blood supply to such an extent that infarction developed. Possibly infection may have played a role, but the microscopical appearance does not particularly encourage the theory of septic infarction.

The tumor was quite well differentiated, obviously slowly growing and very scirrhous in type, I think that it was an adequate explanation of the symptomatology.

itself, although the world still has many more mouths to feed than it has food for, and the dislocations due to war appear to be succeeded by the dislocations due to peace, and now the time seems to have come to consider the righting of some of our older wrongs. A cataloguing of the penalties under which margarine must seek its market furnishes an amazing exhibit.

On the federal side there is a tax of 10 cents a pound on colored and  $\frac{1}{4}$  cent a pound on uncolored margarine. The manufacturer of all margarine must pay an annual federal license fee of \$600. The wholesaler must pay an annual license tax of \$480 to handle colored margarine, and one of \$200 for uncolored margarine. The retailer of colored margarine must pay an annual license fee of \$48, and he who sells uncolored margarine, one of \$6. Public eating establishments, hospitals and charitable, religious and other institutions that serve margarine that they buy and color themselves must pay the yearly manufacturer's license fee of \$600, as well as an excise tax of 10 cents a pound!

So far as state penalties are concerned, nine states, including Connecticut, of the New England group, charge a manufacturer's license fee of \$1 to \$1000 yearly. Fourteen states, including Connecticut and Vermont, charge a wholesaler's license fee of \$1 to \$1000 yearly. Seven states charge an excise tax on all margarine of from 5 to 15 cents per pound. Twelve states, including Connecticut, Vermont and Massachusetts, charge a retailer's annual license fee of 50 cents to \$400. Twenty-four states, including Connecticut, Vermont, Massachusetts, New Hampshire and Maine, bar the sale of colored margarine.

This, if you please, is to stifle the distribution of a highly nutritious, fundamentally inexpensive article of food of which all or part of the ingredients are farm products of forty-four states and that should require no special legislative oversight except, perhaps, that it be served in public under its own name. Government strangles competition the life of trade, and the butter boys sit pretty!

## MASSACHUSETTS MEDICAL SOCIETY

### DEATH

CHURCHILL — Frank S. Churchill, M.D., of Bass River, died February 27. He was in his eighty-second year.

Dr. Churchill received his degree from Harvard Medical School in 1890. Before moving here, he lived in Chicago, where he served as medical inspector on the Board of Health and as chief of staff, Children's Memorial Hospital. He was chairman of the children's section of the American Medical Association and also editor-in-chief of the *American Journal of Diseases of Children*. In 1917-1918, he was chief of medicine at Camp Devens Hospital. He was formerly a medical assistant at the Judge Baker Guidance Clinic, Boston. He was a former president of the American Pediatric Society.

YOUNG — J. Herbert Young, M.D., of Newton, died February 18. He was in his sixty-fourth year.

Dr. Young received his degree from Harvard Medical School in 1906. At the time of his retirement in 1941, he was consultant in pediatrics at the Massachusetts Eye and Ear Infirmary and New England Baptist Hospital, physician to Children's Medical Service, Massachusetts General Hospital, and physician and chief of the Department of Pediatrics, Cambridge Hospital. For many years he was an assistant in pediatrics at the Harvard Medical School. He was a diplomate of the American Board of Pediatrics and a member of the American Academy of Pediatrics and the New England Pediatric Society. He was a fellow of the American Medical Association.

His widow, a daughter and a son survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### BLOOD AND BLOOD DERIVATIVES PROGRAM

#### SURPLUS ARMY-NAVY PLASMA RECEIVED FROM AMERICAN RED CROSS

The Department of Public Health has begun operation of its blood and blood-derivatives program announced in the October 4, 1945, issue of the *Journal*. Collection of voluntary blood donations has been underway, the blood so collected being processed to liquid plasma and plasma fractions, in collaboration with Harvard Medical School pending completion of the Blood Processing Laboratory now under construction in Forest Hills.

The accumulation of an adequate supply of plasma fractions will be greatly facilitated by the recent release of a large supply of surplus Army-Navy dried plasma by the American Red Cross. This plasma is being returned to civilian use throughout the country, with state health departments acting as the distributing agencies.

The first Massachusetts allotment of 15,000 units has been received and will be ready for distribution on March 15, after it has been inspected and checked for condition of packages and date of expiration.

Following consultation with an Advisory Committee consisting of Dr. Elmer S. Bagnall, Dr. Charles A. Janeway, Dr. Charles C. Lund, Dr. Joseph F. Ross, Dr. Michael A. Tighe and Dr. Charles F. Wilinsky, the Department of Public Health has adopted a uniform general policy for handling the distribution of products derived from voluntary human blood donations. The regulations

provement in the general condition of the patients. Only 2 cases were reported as completely cured without surgical drainage, but several of the others were considered to be much better surgical risks as a result of the preliminary treatment with penicillin. Deaths were usually associated with other complicating conditions.

The remaining 236 cases were nonputrid empyemas that were not associated with wounds or operations on the thorax. More than half these cases were cured by aspiration and penicillin treatment without resort to operative drainage. The results reported by different observers vary widely. Several of them obtained results comparable to those of Tillett, whereas a few claimed that operation was necessary in every one of their cases. The type of material available to these workers may have accounted for the differences in the results obtained. It is apparent, however, that the enthusiasm with which the medical treatment was pursued varied considerably, as might be expected with any new form of therapy, and the results varied accordingly.

Jacobson<sup>4</sup> in a recent report from a Navy hospital suggests that the recovery time in patients with empyema whom he treated was actually prolonged by the use of penicillin intrapleurally, although the initial response was good. He concluded that marked thickening of the pleura may follow this treatment and may give rise to deformity and to the impairment of pulmonary function. There is, however, little evidence to support this view. The experiences of Tillett and of the workers at the Boston City Hospital indicate that the time for complete recovery in cases of empyema was considerably shortened if operation was avoided. The final results with respect to impairment of pulmonary function and the residual pleural thickening, as revealed by follow-up x-ray examinations, were at least comparable to, if not better than, those obtained after operative drainage. Additional experience with the medical treatment will be necessary before the end results can be evaluated and compared with those obtained by early resort to surgery.

There can be little doubt in the minds of those who have followed any number of patients with empyema after they had been subjected to rib resection that the results leave much to be desired.

Secondary infection after operation is almost inevitable. Evidence of active infection may last for several weeks, and drainage from the wound may persist for several months before there is complete obliteration of the empyema cavity and healing of the external wound. Ugly scars and deformities of the chest are not infrequent. If a large proportion of cases of empyema can be cured by repeated aspirations and intrapleural penicillin without resort to operation, this method of treatment warrants a serious trial. The end results in terms of the total duration of illness until the cavity is obliterated and all evidence of infection subsides, as well as the residual thickening, the chest deformities and the impairment of pulmonary function, should be carefully assessed and compared with those of surgical drainage before final judgment is passed on the relative value of these forms of treatment.

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#### A BREAK FOR MARGARINE?

DURING the war, when food rationing was in existence and the housewives of America were indoctrinated with the idea of marketing in terms of nutritional values, certain foodstuffs became popularized and were eventually accepted as adequate substitutes for more orthodox articles of diet. The soy bean, as a complete vegetable protein, became a naturalized citizen, oleomargarine, scorned for decades as a result of skilled propaganda on the part of the dairy interests, took its place nearly on a level with butter as a satisfactory table fat.

The *Journal*, in those sober days so recently left behind us, advocated the cause of margarine,\* for despite its acceptance by the open-minded representatives of public opinion, this valuable and potentially inexpensive food still labored under the handicap of various discriminatory and thoroughly undemocratic acts of legislation. Our normal balance of supply and demand is gradually righting

\*Editorial. Food fights for freedom. *New Eng. J. Med.* 230:745, 1944.

## CORRESPONDENCE

MODERN TRENDS IN LOCAL  
BOARDS OF HEALTH

To the Editor Many of the board-of-health members and their agents do not appear to be aware of the current trends in the thinking and planning that is going on for local health work. It is an accepted and well established principle that government is responsible for the health of the people and that certain basic health services should be rendered to all communities, large or small, through a governmental agency.

Two books that have recently appeared, both published by the Commonwealth Fund, are of special value in showing the "way the wind is blowing." *Government in Public Health*, by Dr Harry S. Mustard, is a thoughtful, temperate, review of the evolution of public-health work as a governmental function. It points out the rapidly changing philosophy and action of the federal government in the field of social security and the growing influence it is coming to exercise over state and local work through grants-in-aid. Communities or unions eligible for grants disbursed by the state departments of public health must conform in their health programs and personnel to certain standards and patterns set up by the United States Public Health Service. The other book, *Local Health Units for the Nation*, is a report of a subcommittee of the American Public Health Association by Dr Haven Emerson. This proposes to consolidate all local health organizations in the United States into 1197 jurisdictions, for example, Massachusetts would have 40 jurisdictions. Local boards of health would be abolished. The member of any board can examine the report and see just where his organization fits in, or fits out of, the plan.

It is not a new idea, nor one with which anyone would disagree, that certain basic health services should be provided for all communities, large or small through a governmental agency. Neither is it news that most rural communities and small towns and many larger towns and cities are not receiving proper health services. There are probably not over a score of the 351 communities in Massachusetts that have a first-class up-to-date program carried on by adequately trained persons. If we continue to believe that the people should have this service but do nothing to supply it locally, can we complain if outside force is used to consolidate or combine according to plans that are not entirely agreeable?

It is time that local boards of health woke up to their responsibilities and opportunities. They have both in full measure. Local boards are charged with carrying on an important function of government, and they are given extraordinary police powers and quasi-legal and quasi-judicial powers by state laws to fulfill this function. Yet many board members hardly know what their duties are, and they work under obsolete regulations and place the executive work in the hands of an untrained plumber or a busy practicing physician who can devote little time to his task. Most boards take little or no interest in health legislation that may vitally concern them, such as several bills pending this year in the Massachusetts legislature.

Are boards of health going to do anything about this, or are they going to permit themselves to be abolished and to have the state and federal governments step in and dictate how the goal of basic health activities for all should be provided? Local boards must forfeit some authority. Small communities must pool their interests to make a unit of sufficient size and resources to employ trained people. Subsidies are desirable but local communities should have something to say about any such plan.

Reform or improvement should start with the creation of better boards. Public-spirited citizens who take their duties as public servants seriously and who inquire what their duties are will see the need for improvement and find the way to solve the problem. There are now three ways in which communities may lawfully combine for health work in Massachusetts. Any district health officer knows the answers.

Physicians, as leaders in their communities and as logical candidates for boards of health, should give this serious thought. It is part and parcel of trends in medicine that need study and direction to arrive at the goal that is sought in medical care.

CURTIS M. HILLIARD  
Professor of Biology and Public Health

Simmons College  
Boston 15

FIRST BACTERIOLOGIC LABORATORY  
IN MASSACHUSETTS

To the Editor In the January 10 issue of the *Journal*, an item was published regarding Dr. Francis P. Denny and his retirement as director of health of the town of Brookline. A statement was made that Dr. Denny established the first bacteriologic laboratory in Massachusetts outside Boston. I wish to set up an opposing claim.

I do not wish to detract in any manner from the accomplishments of my friend Dr. Denny. His pioneering in public health and the records in this field that he has earned for himself and Brookline have brought him an outstanding reputation in the Commonwealth and in the Nation, and the unstinted support given him by his community, not only moral but financial, speaks for his leadership in public health. I am sure, however, that Dr. Denny would be the first to disclaim priority to this historical distinction if it was shown to be otherwise.

The *Annual Report* of the Worcester Board of Health for the year 1894 makes the following statement: "To render more certain the diagnosis in cases of diphtheria, the Board of Health with the consent and approval of His Honor the Mayor, established in September last a bacteriologic department [This means September, 1894]."

Since the establishment, the physicians of the city have generally availed themselves of its aid. Dr. Frederick H. Baker, a graduate of Harvard who has given a large amount of time to the study of this branch of his profession, is in charge. At the end of this section of the report it is stated: "We can make claim with pardonable pride for our city that it was the first to inaugurate a department of this character east of New York and one of the first to do so in the country. An establishment of this kind is fast becoming a branch of all well regulated health departments."

This service was a continuing service, as the annual report for 1895 states in regard to diphtheria, "There were 254 cases of this disease reported during the year with 70 deaths, a mortality of 27.55, the first inoculation in Worcester having been made January 5 by Dr. W. T. Clark, chairman of the Board, assisted by Dr. F. H. Baker, its bacteriologist." Dr. Baker continued to conduct the Board of Health Laboratory in the City of Worcester until shortly before his death in 1939.

On this evidence I claim for Dr. F. H. Baker and the City of Worcester the distinction of establishing the first laboratory in the Commonwealth of Massachusetts and in New England, which was second only to one in New York City for the country as a whole.

JAMES O. WAILS, M.D.  
Commissioner of Public Health

Department of Public Health  
Worcester, Massachusetts

We acknowledge the error and accept the correction, our information came from a presumably reliable source. To Worcester goes the distinction of having established the first bacteriologic laboratory in Massachusetts, unless some other municipality can successfully dispute the claim. — Ed

## NOTICES

## ANNOUNCEMENTS

Dr. Herbert Abkowitz announces his return from military service and the reopening of his offices for the practice of medicine and surgery at 599 Broadway, Everett.

Dr. Walter S. Burrage announces his return to the practice of internal medicine and allergy at 330 Dartmouth Street, Boston.

Dr. Philip V. Harrington announces the opening of an office for the general practice of medicine at 28 Pleasant Street, Worcester.

Dr. Hermon Norton, having returned from military service, is opening his office for the general practice of medicine at 56 Pine Ridge Road, Waban.



adopted are given below. The detailed applications of these regulations to plasma distribution are further clarified where indicated.

1 Regulations for distribution and use of products derived from voluntary blood donations will be made by the Department of Public Health, following consultation with representatives of the Massachusetts Hospital Association, the Massachusetts Medical Society and an advisory committee of physicians experienced in the study and use of blood and blood derivatives.

2 Recommended uses for products will be defined by the department, after consultation with consultants. Use of products for conditions other than those recommended may be authorized by a regional consultant designated by the department.

The supply of plasma is not unlimited, and its use will therefore be restricted for the present to the emergency control of shock associated with trauma, acute hemorrhage, burns and other surgical or medical emergencies.

3 Distribution will be handled through the Division of Biologic Laboratories, Department of Public Health, which may establish depots at designated points in the Commonwealth.

Initial plasma shipments will be made from the Division of Biologic Laboratories, 375 South Street, Jamaica Plain 30, directly to licensed hospitals throughout the state. All hospitals are being notified that the plasma is available. Arrangements will be made at a subsequent date for distribution of plasma through a small number of regional distribution centers. To provide for major emergencies in the western part of the Commonwealth, an ample reserve of plasma is being transferred for storage in that area.

The initial shipments to general hospitals will be made on the basis of 1 unit of plasma for every four beds, the minimum shipment being 6 units. Initial allotments for chronic or special hospitals will be based on anticipated needs for two months, which should be indicated in requests. The recommended minimum stock for general hospitals is 1 unit for every ten beds or 6 units, whichever is larger. Replacement orders should be calculated to supply one month's needs. Replacements will not be shipped oftener than once a month except in emergencies. As nearly as possible, shipments will be made in case lots.

4 Products may be secured from the Division of Biologic Laboratories or from a depot by a hospital, a physician or an authorized representative of the above on signing a receipt. Certain designated products may also be distributed through boards of health.

Plasma may be issued from a hospital supply to a licensed physician or his representative on signing a receipt. Duplicates of such receipts are to be forwarded to the Division of Biologic Laboratories.

5 Products will be available to all physicians licensed to practice in Massachusetts, under the provisions outlined below.

6 No charge for the products may be made to the patient or at any step in their distribution. This provision does not preclude a reasonable charge for their administration to a patient.

7 Reports of the use of products are to be made out on the forms to be provided, and returned to the Division of Biologic Laboratories for study. Future development of distribution policies, clinical uses and investigation of new developments in blood products will be based on these reports.

The Army-Navy report form inside the package should be discarded. The Department of Public Health is furnishing a report form-postcard with each package. Physicians using plasma are urged to supplement these reports with letters regarding any subsequent reactions that may appear several months after the use of plasma. Any possible occurrence of homologous serum jaundice should be specifically reported, since it is of extreme importance to evaluate the significance of this complication of the use of plasma on a large scale.

## COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JANUARY, 1946

### RÉSUMÉ

DISEASES	JANUARY 1946	JANUARY 1945	SEVEN YEAR MEDIAN
Anterior poliomyelitis	0	2	0
Chancroid	3	3	*
Chicken pox	1023	1798	1798
Diphtheria	10	18	18
Dog bite	499	594	511
Dysentery, bacillary	4	43	20
German measles	73	156	130
Gonorrhea	663	366	357
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	10	*
Malaria	52	68	1
Measles	1018	260	1647
Meningitis meningococcal	25	18	13
Meningitis, Pfeiffer-bacillus	3	7	4
Meningitis, pneumococcal	3	5	8†
Meningitis, staphylococcal	0	0	0†
Meningitis streptococcal	1	0	0†
Meningitis, other forms	6	2	2†
Meningitis undetermined	4	5	7†
Mumps	698	2010	913
Pneumonia lobar	325	300	618
Salmonella infections	5	3	4
Scarlet fever	811	1618	1200
Syphilis	617	358	400
Tuberculosis pulmonary	269	213	213
Tuberculosis other forms	6	12	18
Typhoid fever	0	0	4
Undulant fever	1	2	2
Whooping cough	480	612	881

\*Made reportable December 1943

†Four-year average

### COMMENT

Scarlet fever, diphtheria, mumps, measles and German measles were all reported at figures definitely below their seven-year medians, although record low figures were not approached.

Chicken pox was reported at the lowest figure in January of any corresponding month since 1923.

Pneumonia cases for the month were second only to the record low figures of January, 1945.

### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Diphtheria was reported from Boston, 3, Brockton, 1, Chelsea, 1, Lowell, 1, New Bedford, 2, Pembroke, 1, Taunton, 1, total, 10.

Dysentery, amebic, was reported from Camp Edwards, 1, Waltham Regional Hospital, 1, total, 2.

Dysentery, bacillary, was reported from Lowell, 2, Springfield, 1, Waltham Regional Hospital, 1, total, 4.

Encephalitis, infectious, was reported from Easton, 1, Milford, 1, total, 2.

Malaria was reported from Arlington, 1, Attleboro, 1, Boston, 19, Cambridge, 3, Camp Edwards, 3, Everett, 2, Fort Devens, 5, Gardner, 1, Haverhill, 1, Lawrence, 1, Natick, 1, New Bedford, 1, Newton, 2, Plymouth, 1, Quincy, 1, Salem, 2, Somerville, 2, Waltham Regional Hospital, 2, Worcester, 3, total, 52.

Meningitis, meningococcal, was reported from Arlington, 1, Barnstable, 1, Boston, 2, Brimfield, 1, Brookline, 1, Cambridge, 1, Dracut, 1, Fall River, 1, Framingham, 1, Groveland, 1, Lowell, 1, Lunenburg, 1, Malden, 1, Newton, 1, North Attleboro, 1, Quincy, 3, Springfield, 1, Watertown, 1, Wenham, 1, Weymouth, 1, Winchendon, 1, Worcester, 1, total, 25.

Meningitis, Pfeiffer-bacillus, was reported from Reading, 1, North Attleboro, 1, Worcester, 1, total, 3.

Meningitis, pneumococcal, was reported from Boston, 1, Northboro, 1, Quincy, 1, total, 3.

Meningitis, streptococcal, was reported from Wareham, 1, total, 1.

Meningitis, other forms, was reported from Boston, 4, Milton, 1, Taunton, 1, total, 6.

Meningitis, undetermined, was reported from Boston, 1, Camp Edwards, 1, Northampton, 1, Webster, 1, total, 4.

Salmonella infections were reported from Boston, 1, Cambridge, 1, Hingham, 1, Melrose, 2, total, 5.

Septic sore throat was reported from Boston, 5, Brockton, 1, Cambridge, 1, Fall River, 1, Medford, 1, North Adams, 1, total, 10.

Trachoma was reported from Chicopee, 1, total, 1.

Trichinosis was reported from Boston, 2, Wellesley, 1, total, 3.

Undulant fever was reported from Lenox, 1, total, 1.

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## THE REPAIR OF CRANIAL DEFECTS WITH SPECIAL REFERENCE TO THE USE OF CANCELLOUS BONE\*

COMMANDER JOHN T. B. CARMODY (MC) U. S. N. R. †

THE treatment of defects of the cranial bones is a problem as old as cranial surgery. All types of material have been used, and the search for a completely satisfactory substance continues. The war has stimulated such endeavor, and there is no doubt that vast strides have been made. There has been a strong tendency toward the use of metal. Almost all metals have been tried in one form or another, each having its advocates and showing advantages over the others, but each possessing distinct disadvantages. Formerly, the most successful and most popular materials were silver and vitallium,<sup>1</sup> but other substances such as celluloid have had their followers. The repair of large cranial defects by silver plates has been successful for varying periods of time, but the majority of such plates have had to be replaced. Generally speaking, the use of silver is a thing of the past. In 1937, it was noted that vitallium caused only negligible tissue reaction and gave evidence of great promise,<sup>1-4</sup> but it was difficult to work with, and although still used this material has been superseded by tantalum.<sup>5-7</sup>

Burch, in 1938, first saw the surgical possibilities of tantalum,<sup>7</sup> and Pudenz,<sup>8</sup> in 1942, emphasized its future in neurosurgery in a paper on tissue tolerance of the metal in cats. It was also shown that a thin, filmy, translucent, gelatinous membrane enveloped the metal within forty-eight hours, thus tending to prevent fixation to the nervous tissue.<sup>9</sup> On the other hand, some question has arisen through the experiments of Delarue,<sup>10</sup> who, working with dogs, proved that tantalum could become attached to the cerebral cortex by firm adhesions and that the adjacent arachnoid and dura could become thickened. Recently, Robertson and Peacher<sup>11</sup> have found no such indication of tissue reaction in human beings, but there is evidence that such a complication may occur, as indicated in one of the cases reported in this paper.

Nevertheless, tantalum has been and continues to be the most satisfactory metal used in cranioplasty. It is light, nonmagnetic and chemically inert, is easily molded and does not require preliminary casting. It is soft enough so that drill holes can easily be placed at the time of operation, and no special instruments are necessary to handle it. In summary, tantalum offers inertness, mobility and strength—three factors not present in the metals previously used.

In the matter of basic requirements for an alloplastic material, it appears that the goal has been reached. Recently, several impressive series of cases receiving cranioplasty have appeared in the literature.<sup>9, 12, 13</sup> The immediate results in many cases have been remarkable, but in spite of initial perfection, some evidence is accumulating that tantalum is not suitable in all cases. Heavily scarred areas that have remained intact for varying periods have gradually broken down, and once this process has begun, the basic inertness of the metal does not prevent it from being extruded like any foreign body. Again, the possibility of cortical fixation has not been completely disproved. Other disadvantages are gradually taking shape, such as the preclusion by a plate of any future x-ray studies. It is true that some of these disadvantages may arise from the technical difficulties of cranioplasty rather than from the metal itself. Also, it cannot be denied that the result of enthusiasm for cranioplasty has been that many cranial defects have been subjected to so-called plating that in former years and under different circumstances would have been let alone. Significantly, in this group are found cases with more complaints following repair than before it. Much has been written concerning the indication for cranioplasty, and almost any case of skull defect can be made to meet such requirements.<sup>6, 12, 13</sup>

It seems more to the point to emphasize the contraindications. The clinical cases exhibiting them fall into two main categories—those with a simple "hole in the head" associated with no complaints, and those in which the complaints are consistent with functional involvement. There

\*This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

†Neurosurgeon, Worcester City and Worcester Memorial Hospitals, and Assistant in neurosurgery, Massachusetts General Hospital (on leave of absence).

Dr Calvert Stein announces his return from military service and resumption of practice of psychiatry and neurology at 175 State Street, Springfield

Drs John W Strieder, Dwight E Harken and Joseph P Lynch announce the removal of their office from 171 Bay State Road, Boston, to 1180 Beacon Street, Brookline

Dr Charles L Swan, Jr., announces his return to the practice of surgery at 20 Gloucester Street, Boston 15

Dr Channing S Swan announces his return to the practice of urology at 20 Gloucester Street, Boston

Dr Jacob H Swartz announces that Dr Earl A Glicklich, having recently returned from active service, will be associated with him in the practice of dermatology and syphilology at 371 Commonwealth Avenue, Boston

#### MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

A dinner meeting of the Middlesex South District Medical Society will be held at the Hotel Continental, Cambridge, on Wednesday, March 20, at 6 00 p m. Veterans of the district will be guests of the society. Others are welcome on payment of \$5 for dinner. The fees should be sent to Dr Fabyan Packard, 245 State Street, Boston. Dr E D Churchill will be the speaker, and Dr Harold Giddings will act as toastmaster.

#### SOUTH END MEDICAL CLUB

The next meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, March 19, at twelve noon. Dr Moses H Lurie will speak on the subject "Deafness and a Few of the Emergencies in Ear, Nose and Throat." Dr H S Card will preside.

Physicians are cordially invited to attend

#### UNITED STATES PUBLIC HEALTH SERVICE

Examinations for appointments of medical officers in the Regular Corps of the United States Public Health Service will begin on April 4 at various convenient localities throughout the country. Examinations are for appointments to fill vacancies of assistant surgeon (first lieutenant) and senior assistant surgeon (captain).

Regular Corps appointments are permanent. They provide qualified doctors with opportunities for a career in one or more of a number of fields including research, general hospitals, special hospitals, foreign duty and public-health programs. Assignments are made according to careful consideration of the officers' demonstrated abilities and experiences. It is expected that doctors now leaving the armed services will find the openings of particular interest.

Entrance pay for assistant surgeon with dependents is \$3411 a year, and for senior assistant surgeon with dependents is \$3991 a year. Promotions are at regular intervals up to and including the grade of medical director, which corresponds to full colonel at \$7951 a year. Retirement pay at the age of sixty-four is \$4500 a year. Full medical care, including disability retirement at three-fourths pay, is provided. All expenses of official travel are paid by the Government. Thirty days' annual leave with pay is provided.

An applicant for the grade of assistant surgeon must be a citizen of the United States, must present a diploma of graduation from a recognized medical school, must have had or be in the process of completing the seventh year of college or professional training or experience since high-school graduation (two years premedical, four years of medicine and one year internship) and must have a physical examination at the place of oral examination by medical officers of the Service.

An applicant for the grade of senior assistant surgeon must meet the above requirements and must have had four additional years of postgraduate training or experience.

Examinations will be oral and written. The written examination will be held on May 14, 15 and 16 at places convenient to the candidate and the Service. National Board grades may be used for the assistant-surgeon examination. The oral examination will be held at 9 a m at the places and dates listed below.

Atlanta, Georgia — Malaria Control in War Areas, 605 Volunteer Bldg.	Apr 22
Baltimore, Maryland — Marine Hospital, Wyman Park Drive and 31st Street	May 9
Boston, Massachusetts — Marine Hospital, 77 Warren Street (Brighton)	May 6
Chicago, Illinois — Marine Hospital, 4141 Clarendon Avenue	Apr 30
Cleveland, Ohio — Marine Hospital, Fairhill Road and E 124th Street	May 1
Denver, Colorado — 617 Colorado Bldg.	May 3
Detroit, Michigan — Marine Hospital, Windmill Pointe	Apr 8
Fort Worth, Texas — U S Public Health Service Hospital	May 2
Kirkwood, Missouri (near St. Louis) — Marine Hospital, 525 Couch Ave.	Apr 25
Los Angeles, California — U S P H S Relief Station, 406 Federal Building	Apr 26 27
Minneapolis, Minn — Office of Indian Affairs, 218 Federal Office Bldg.	Apr 9
New Orleans, Louisiana — Marine Hospital, 210 State Street	Apr 29
New York, New York — Marine Hospital, Stapleton, Staten Island	Apr 23, 24
Norfolk, Virginia — Marine Hospital, Hampton Blvd, Larchmont	May 7, 8
San Francisco, California — Marine Hospital, 14th Ave and Park Blvd	May 10
Seattle, Washington — Marine Hospital, Judkins St and 14th Ave. South	Apr 10 11
Washington, D C — U S P H S Dispensary, Fourth and D Streets SW	Apr 12, 13
	Apr 4
	May 13

Application forms may be obtained by writing to the Surgeon General, United States Public Health Service, Washington 25, D C

#### NORTON MEDICAL AWARD

The book-publishing firm of W W Norton and Company announces that it is again inviting manuscripts for submission to be considered for the Norton Medical Award of \$3500 offered to encourage the writing of books on medicine and on the medical profession for the layman. The first such award was made to *The Doctor's Job*, by Dr Carl Binger, published last spring, which gave the doctor's point of view on his work. Announcement will be made shortly of the winning book for 1946. Closing date for submission of manuscripts this year is November 1. All particulars relating to requirements and terms may be had by addressing W W Norton and Company, Incorporated, 70 Fifth Avenue, New York 11, N Y.

#### SOCIETY MEETINGS AND CONFERENCES

##### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MARCH 21

###### FRIDAY, MARCH 22

\*9-00-10-00 a m First Stages of Human Conception Dr John Rock Joseph H Pratt Diagnostic Hospital

\*10-00 a m-12-00 m Medical Staff Rounds Peter Bent Brigham Hospital

10 50 a m Electrodesiccation and Electrocoagulation in Diseases of the Skin Dr S J Messina (Postgraduate Clinic in Dermatology and Syphilology) Amphitheater, Dowling Building Boston City Hospital

###### MONDAY, MARCH 25

\*12-00 m-1-00 p m Clinicopathological Conference Peter Bent Brigham Hospital

###### TUESDAY, MARCH 26

\*12 15-1 15 p m Clinicorontgenological Conference Peter Bent Brigham Hospital

###### WEDNESDAY, MARCH 27

\*9-00-10-00 a m Roentgenological Changes in Sprue and Other Nutritional Disturbances Dr Alice Ettinger Joseph H Pratt Diagnostic Hospital

\*10 30-11 30 a m Medical Clinic Isolation Building Amphitheater Children's Hospital

(Notices continued on page xix)

doomed from the beginning. Consequently, a section of the plate underlying the main scar areas was removed. This allowed the soft-tissue edges to overhang the plate but in periphery which was adherent to the dura. Whether this picture was entirely the result of the infection could not be determined. The scalp was firmly attached to the plate in



FIGURE 3 Case 1  
*This film is a right lateral view that was taken three months postoperatively. The graft is solid, and the inner bone surface, as seen in the stereoscopic films, forms a smooth and even contour.*

site of tissue contact, further recession with attempted extrusion of the plate ensued, and as a result it was surgically removed. At the time it was noted that a multiloculated space, some areas being fully 2 cm. in depth, lay between a different manner than has been noted with nonperforated plates. The only form of treatment for the next several weeks was frequent irrigations with penicillin. The multiloculated

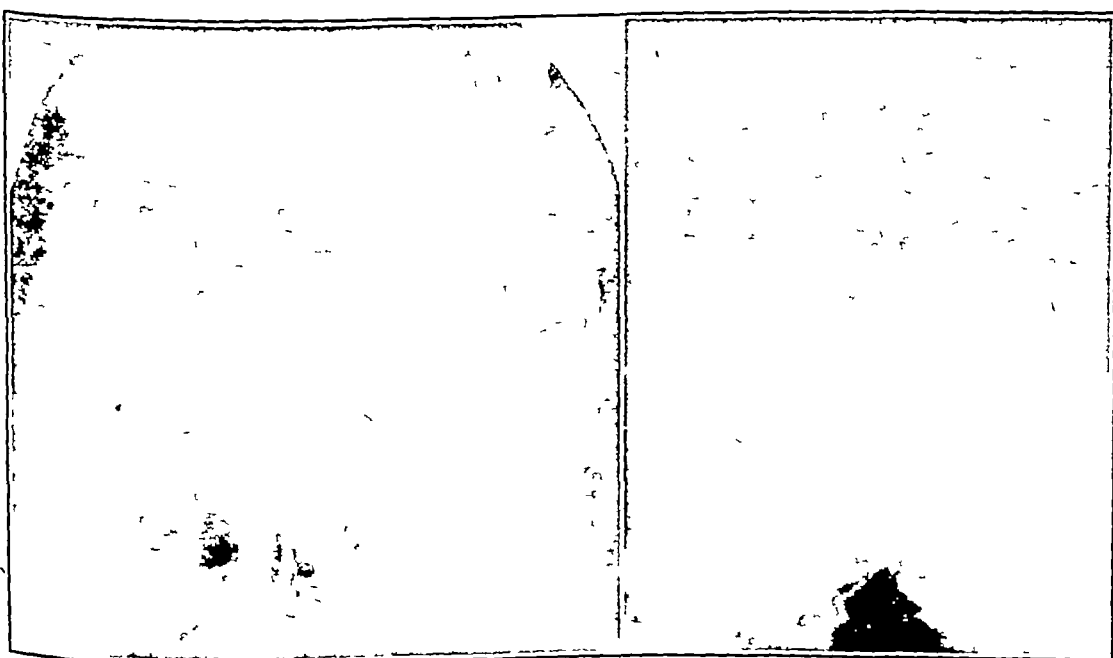


FIGURE 4 Case 2  
*A is a film showing the tantalum plate in position over the skull defect, the left frontal sinus is less distinct than the right one. B is a film taken two months after operation, the graft was firm and solid and had effected the proper contour to the forehead.*  
the plate and the intracranial structures and encompassed the entire undersurface of the plate. This space was partitioned by thin tissue bands, with the exception of the frontal space gradually filled in. X-ray examination showed no evidence of bone infection. A bone graft of cancellous chips from the ilium was de-

are, of course, other minor groups of cases, such as those with sizable retained foreign bodies, in which



FIGURE 1 Case 1

*This shows the condition of the patient's wound on admission. The presenting portions of the perforated plate are readily seen. It illustrates the manner in which the heavily scarred, thinned-out areas break down. Three days later the rest of the scar gave way.*

the advisability of cranioplasty is questionable. Opinion concerning its value when epilepsy is present is divided. At one extreme, Gardner<sup>12</sup>

reported has not been sufficient to warrant any definite conclusion, and although some suggestive improvement has occurred, it must be remembered that a cranial procedure of any type frequently effects a temporary change in the convulsive state.

The following 2 cases are summarized to illustrate some of the inadequacies of tantalum. They are presented not from the point of view of criticism of treatment but in an attempt to show that the use of bone in cranioplasty is not obsolete and that in certain cases this material should in fact be the one of choice.

### CASE REPORTS

**CASE 1** A 29-year-old veteran, was admitted to the hospital on February 16, 1945, with a diagnosis of meningitis. He complained of severe headache, a draining head wound and a stiff neck. He had been wounded in the head by a bomb fragment on September 23, 1943, and had developed successively a herniation of the right frontal cerebral hemisphere, right frontal osteomyelitis and epilepsy. Subsequently, several operations had been performed, including as a final procedure the insertion of a large tantalum plate. The patient was discharged from the service on January 8, 1945, at which time his general condition was excellent. The head wound had completely healed. During the next month, he experienced slight headaches and a feeling of tightness involving the right frontal region. These symptoms increased in severity and culminated in the breaking down of a portion of the heavily scarred scalp.

Physical examination on admission showed an acutely ill patient. The temperature was 101°F, and the pulse 110. The neck was slightly rigid, and a profuse thin, purulent discharge was issuing from the several presenting perforations in the exposed areas of the tantalum plate (Fig 1). The remainder of the examination was negative with the exception of a left-sided hyper-reflexia. Cultures were positive for a hemolytic staphylococcus.

The infection was readily controlled by chemotherapy, but further breakdown of the scar continued. X-ray examination showed a large and exceptionally well molded

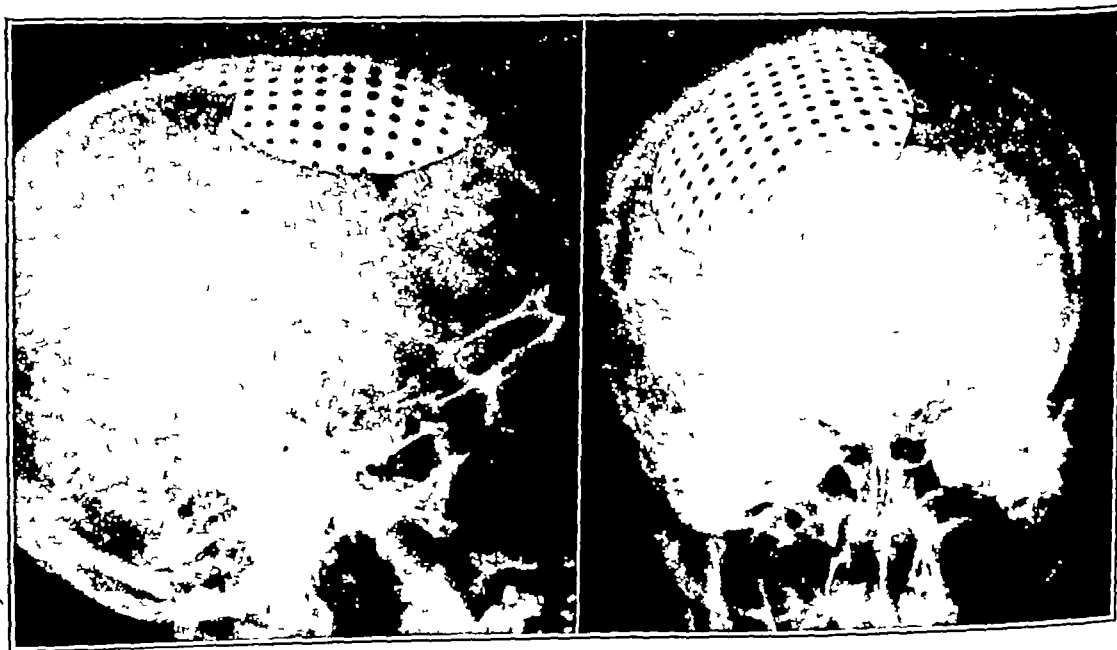


FIGURE 2 Case 1

*These films show the size of the tantalum plate. Many old fracture lines remain visible, indicating the extensiveness of the original injury.*

believes that cranioplasty has been most beneficial. The time interval in the series of cases subsequently

and fitted tantalum plate (Fig 2). It was decided to save as much of the plate as possible. It seemed to be a foregone conclusion that a subsequent total cranioplasty would be

not to pierce through the scarred area to its external surface. This is an extremely easy thing to do, and is almost certain to result in tissue breakdown postoperatively. When the lower margin of the defect has been exposed and completely freed, all bleeding points — and there are often many, depending on the size and character of the scar — may be controlled more completely and easily with fibrin foam-packs than by any other combination of methods. Freshening up the bony edge around the defect should be avoided. The danger of diploic bleeding outweighs any suspected advantage that such a procedure may have.

With the bed prepared and all bleeding controlled, cancellous chips approximately 1 cm in diameter are placed in mosaic layers, entirely filling the defect. Chips of this size are readily obtained by biting them off from the graft with a rongeur. As a final step, when possible the periosteum surrounding the exposed bone defect is incised and turned back over the borders partially enclosing the cancellous chips. Mowlem<sup>14</sup> believes that this is not necessary and prefers to have the chips in direct contact with the denuded bone. The scalp flap is sutured and a light compression dressing is applied.

Postoperatively, formation of a hematoma occasionally occurs in spite of the utmost precautions before closure. Local application of heat accompanied by drainage at the most dependent region of the incision, results in quick resolution. When an extensive loss of underlying soft tissue has occurred, the original scar may break down. Irrigation with penicillin in a 1:1000 concentration is followed by rapid healing. This result is a decided contrast to the problem that arises when metal of any kind is used as the underlying material.

So far as the graft is concerned, firm union is present clinically in two or three weeks. Generally the x-ray picture in the early stage is that of intact and living bone without confirmatory evidence of union. The proper contour of the graft is readily maintained by the pressure of the overlying scalp against the easily molded mass of cancellous chips. Contour adaptability of the graft is the greatest single advantage of this method. The fact that Mowlem<sup>14</sup> has had marked success in extensive facial-bone defects emphasizes the ease with which cancellous bone can be molded to fit the occasion.

That absorption of some elements of the graft may take place cannot be denied. This has occurred in some of this series of cases, but in none to the extent that the graft has lost its primary point of obliterating the defect. Actually, when absorption did take place only the chips that could be considered excessive were singled out, and in such a manner that the graft gradually progressed in contour and thickness to that of the normal adjacent bone.

The method of taking the graft is simple and

can be carried out in a few minutes. The crest of the ilium is exposed and the flat surface of the bone is laid bare. The outer cortical layer is split with a rotary bone saw and turned down. Thin strips of the medulla are sliced free and when a sufficient amount has been obtained the cortical layer is replaced and sutured into its former position. The hip wounds heal quickly, and there have been no complications or complaints other than soreness for the first two or three days.

### DISCUSSION

It is not the purpose of this paper to condemn or undermine the use of tantalum in cranioplasty, but rather to advance the cause of cancellous-bone grafting in selected cases. An attempt has been made to show that cancellous bone may be the material of choice under certain circumstances and that its use should not be relegated to the past.

It is difficult to conceive of cancellous bone's fulfilling satisfactorily the obligation of repair either in exceptionally large defects or in those whose location precludes its use. With respect to



FIGURE 6 Case 3

*This is a photograph of the patient taken two weeks postoperatively. The defect in the left orbital ridge and frontal sinus has been corrected.*

the first type of case, the use of cancellous bone must be self-limiting. Sufficient bone to repair small and medium-sized defects is readily obtained from the ilium, as outlined above, whereas to take the amount of bone required for the larger defects would transform a minor procedure into one of major proportions. In defects of the orbital ridge and frontal sinuses, tantalum seems preferable, although Mowlem<sup>14</sup> has used cancellous bone in this location with excellent results. Figures 5 and 6 depict a problem of this type.

cided on and was carried out. Prompt healing followed, and the last x-ray film showed that the graft was intact and united (Fig 3). At the present time the patient has no complaints referable to the head. Clinically the grafted area is sound. There is no pulsation, and the patient no longer feels as though, in his words, something were in his head that did not belong there.

**CASE 2** A 20-year-old seaman was admitted to the hospital on May 8, 1945, with the complaints of headache and of swelling and tenderness in the left frontal region. He had had a frontal sinusitis on August 29, 1944, and had subsequently developed a left frontal brain abscess. The abscess was drained on November 5, and a small tantalum plate

preparation of the site of the bone defect is concerned. There are, however, several points that must be observed if rapid healing is to occur. In the first place, all scarred areas should be carefully avoided in making the incision, unless they are of such size and location that they can be resected at the time. In many cases the fractures have been extensively compounded, with severe loss of soft tissue, resulting in heavy scar formation and fixation to the underlying tissues, including the dura

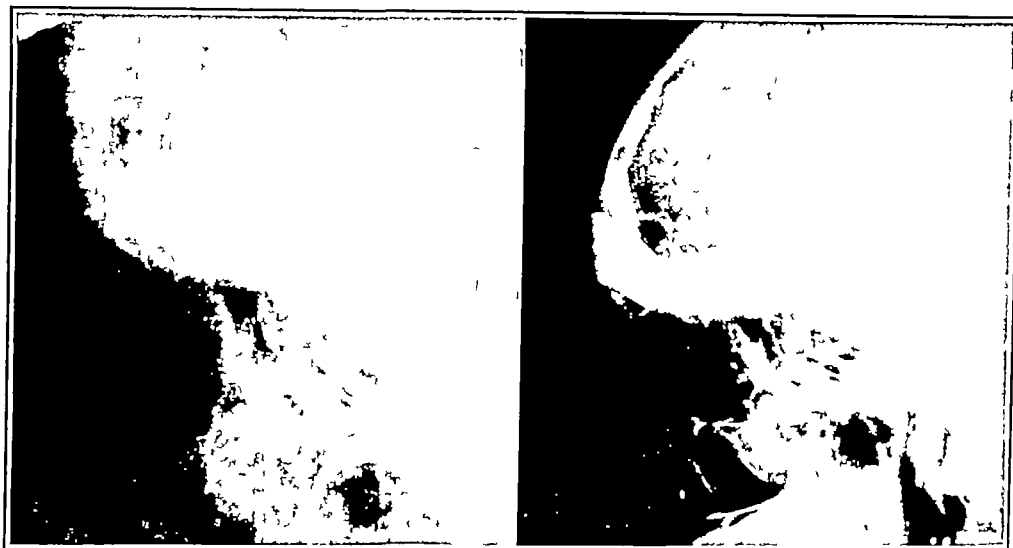


FIGURE 5 Case 3

*A shows a defect of the left orbital ridge and frontal sinus, with an unsatisfactory attempt at repair with bone, the bone graft was loose, sagged into the soft tissues of the orbit, with marked deformity, and caused severe pain due to tension on the supraorbital nerve. B is a film taken after removal of the graft and repair of the defect by a contour-fitting tantalum plate.*

was inserted to prevent deformity. The patient showed prompt and immediate improvement and was discharged to full duty on April 26, 1945.

On admission he stated that he had been well except when he "caught cold." With the onset of each upper respiratory infection, he noted severe headache, swelling and tenderness about the site of the operation. These attacks at first subsided within a few days, but the last one was severe and resulted in admission to the sick list.

Physical examination showed an acutely ill young man. There was moderate swelling of the entire left frontal area. The tantalum plate could be palpated, and there was marked tenderness about its edges. There were no abnormal neurologic signs. The spinal fluid was within normal range with the exception of the pressure, which was equivalent to 250 mm of water. X-ray examination showed the presence of a small tantalum plate (Fig 4A). The lateral film suggested that the plate might be riding, and this was confirmed by the onset of pulsations with the regression of the swelling.

Conservative treatment was carried out until the acute phase of the infection had subsided. At operation on June 6, 1945, the plate was found to be riding and was removed. At the same time the defect was repaired with cancellous bone from the ilium. On the 6th postoperative day pulsations had ceased. Within 2 weeks the graft was firm, and the final film, taken 2 months later (Fig 4B) showed the bone graft to be intact and united firmly with the surrounding bone. The patient was followed for 2 months and remained free of complaints.

The operative technic in this procedure does not differ from that of any other method so far as the

or the cortex. When such areas, or even minor portions of them, have been included in the incision, some degree of incisional breakdown invariably follows. In many cases it is not feasible to attempt plastic correction of scarring as a preliminary step to defect repair, because of the extensive and complete adherence of the intracranial tissues to the overlying structure. Many patients have undergone several operative procedures, and the advisability of any further preliminary plastic repair before that of the defect has been accomplished is questionable. The treatment of these scars may be a major problem and is in itself a subject requiring separate attention.<sup>13</sup> Finally, the wound should be completely healed before grafting is done. Occasionally, in exceptionally involved defects, as in Case 1, this is not possible. In this event, convalescence is lengthened and the danger of bone absorption is increased.

Following the making of the flap incision, the aponeurosis is dissected from the periosteum to the edge of the bone defect, and the scar, which may begin at the margin of the defect, is carefully dissected from the dura. It is most important

is that of all methods of repair cancellous-bone grafting is certainly the simplest and easiest. Plating by mortising the periphery of the bone defect may be an undertaking of considerable magnitude.<sup>15, 16</sup> Fixation or wedging is simple when the exposure is easily achieved, but with involvement of the squamous portion of the temporal bone, even these methods become complicated. When impressions of the defect are made for casting, a two-stage operation is the rule. Simple fixation by tantalum screws reduces the operation to the level of grafting, but here again such a method is not always applicable.

Attention must be called to the fact that other materials than metals are being used in cranioplasty. Methyl acrylic, with which we have had no experience, is receiving support by its advocates,<sup>17</sup> but its use also requires a longer procedure and a more elaborate setup. That it has any outstanding advantages over tantalum, with the exception of its being radiolucent, seems doubtful.

Recently, Mowlem<sup>14</sup> has published a series of 75 cases of bone grafts in which cancellous chips were used exclusively. In most of the cases dealt with there were facial and long-bone defects, but there was 1 case of frontal-bone defect in which complete clinical healing with firm union occurred in ten days. This case has been followed for three years, during which period the graft has remained solid, with no evidence of absorption.

Mowlem attributes the marked success of cancellous bone for grafting to its highly vascular character. He believes further that fragmentation is a definite aid in the survival of these grafts on the theory that a greater proportion of the bone cells becomes accessible to early vascularization.

The chief objections in the past to the use of bone in defect repairs — namely, the extensiveness of the operation, often necessitating two stages, and the extreme difficulty of obtaining the proper contour effect — have been overcome by the use of cancellous bone. Furthermore, if the size of

the cranial defect is kept at a minimum at the time of the initial débridement, as has been frequently advocated, many unnecessarily large defects requiring the use of alloplastic materials can be avoided.<sup>17, 18</sup> This in itself as a preventive measure would do much to reduce the number of cases requiring extensive cranioplastic measures.

## CONCLUSIONS

Autogenous cancellous bone is the material of choice in small and medium-sized defects of the skull requiring cranioplasty.

The repair of cranial defects with tantalum is at present the procedure of choice when the defects are of such size that a sufficient amount of bone cannot be obtained without an extensive secondary procedure, or when the site of the defect renders tantalum the more suitable material.

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On the other hand, in both simple and complicated medium-sized defects of the vault, cancellous-bone grafting is in every particular the best method. The last 7 cases receiving cranioplasty in this hos-

pital have been treated in this manner, and with one exception healing has been prompt. In the excepted case, there was a minor breakdown of tissue involving a portion of the original scar. Ir-

coincidental subsidence of the defect caused by the complaints. In defect areas in which deformity had been marked, proper and satisfactory contour healing occurred, Figures 7 and 8 illustrate such a



FIGURE 7 Case 4

*These photographs show a medium-sized defect, with contour deformity, in the right frontal bone*

pital have been treated in this manner, and with one exception healing has been prompt. In the excepted case, there was a minor breakdown of tissue involving a portion of the original scar. Ir-

case. Furthermore, some patients with plates have said that they are constantly aware of the presence of a foreign body—in their own words, “something that does not belong there.” It seems logical

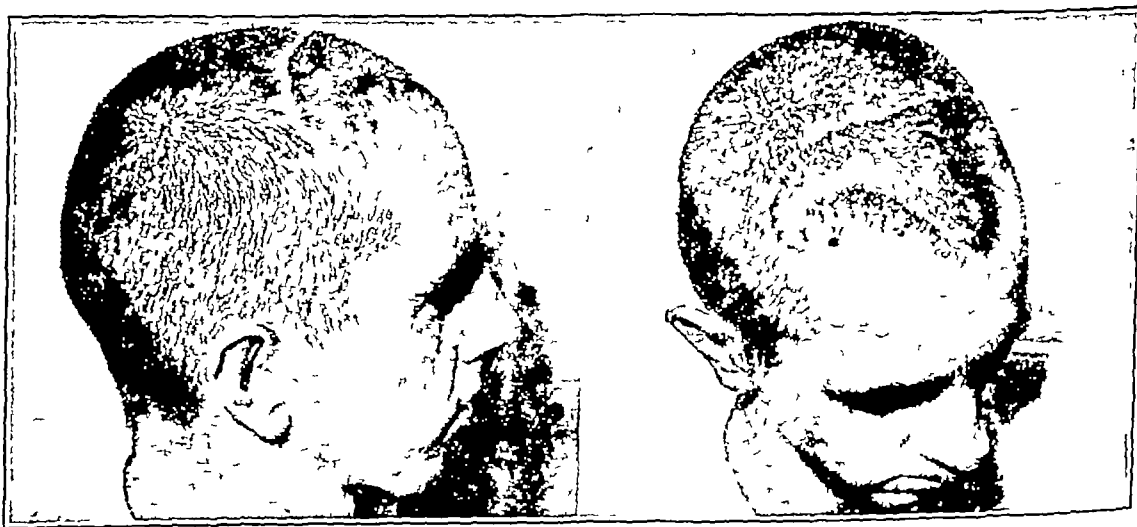


FIGURE 8 Case 4

*These photographs were taken two weeks following a cranioplasty with cancellous bone. The contour deformity had been corrected, pulsations had ceased, and the graft was solid.*

rigations with penicillin were used, and rapid healing occurred. In all cases the grafts were clinically solid within two or three weeks. Defect pulsation disappeared in approximately one week, with a

to assume that no matter how inert a material may be it is still a foreign body, and if its presence can be avoided by the use of autogenous material, this should be employed. Another factor of importance

developed this symptom shortly after childbirth (Table 3)

A good deal of evidence, however, can be cited against the assumption that exertional incontinence



FIGURE 1

*This patient had a reversed urethral curve. She had never been pregnant and had had no incontinence*

invariably results from obstetric trauma. Typical exertional incontinence may occur without pregnancy or pelvic delivery, as shown by the case histories of the 5 nulliparas and 2 patients delivered by cesarean section. Trauma is therefore not a prerequisite for the development of urinary incon-

tion between trauma and the ensuing symptoms, which establishes their causal relation. This is not so with exertional incontinence. The extent of obstetric damage to the pelvic and perineal structures cannot be correlated with the degree of urinary leakage. Moreover, in the average case nine years are found to have elapsed before the patient first



FIGURE 3

*This patient had prolapse of the uterus and a cystocele but no incontinence*

noted loss of urine on coughing or sneezing. Many women do not become aware of poor urinary control until fifteen to twenty years after the birth of the



FIGURE 2

*This patient had a large cystocele. There was a wide urethra and slight "funneling" of the internal sphincter, but no incontinence*

tinence. The symptom complex, moreover, lacks the clinical attributes of a so-called "traumatic lesion." The sequelae of trauma are usually in direct proportion to the extent of injury. Thus,

TABLE 3 The Onset of Incontinence in Relation to Parturition (90 Cases)

INTERVAL BETWEEN CHILDBIRTH AND ONSET OF INCONTINENCE	PERCENTAGE OF CASES
37	
Less than 1	26
1-4	10
5-9	10
10-14	22
15-19	16
20-24	17
25 and over	4
	5

the greater the injury, the more widespread are the effects. Furthermore, there is a definite time rela-

tion between trauma and the ensuing symptoms, which establishes their causal relation. This is not so with exertional incontinence. The extent of obstetric damage to the pelvic and perineal structures cannot be correlated with the degree of urinary leakage. Moreover, in the average case nine years are found to have elapsed before the patient first

noted loss of urine on coughing or sneezing. Many women do not become aware of poor urinary control until fifteen to twenty years after the birth of the last child, or indeed not until the menopause. This long time interval between cause and effect is not in keeping with experience in traumatic lesions elsewhere in the body and suggests strongly that the two are not causally related.

A urethral lesion pathognomonic of exertional incontinence, moreover, has proved to be elusive. Evidence of its existence has been rather involved and indirect. Considerable interest has recently been evoked by Kennedy's<sup>1-4</sup> suggestion that fixation of a middle urethral sphincter by scar tissue causes exertional incontinence. No such specific lesion or deformity, however, was found on careful study among the 95 patients of this series. Furthermore, the sphincter to which Kennedy refers has never been demonstrated anatomically, and it is doubtful that one thus situated could be of any great

LACK OF A SPECIFIC URÉTHRAL LESION IN EXERTIONAL URINARY INCONTINENCE\*

S RICHARD MUELLNER, M D †

BOSTON

IT IS generally believed that exertional urinary incontinence is due to trauma of childbirth. Although there is no agreement on the precise structure that has been injured, prevailing opinion ascribes this symptom to tears or fixations of the urethral sphincters or to attenuations of the bladder and urethral supports. The signs of obstetric trauma, however, are often not discernible on pelvic examination or at operation, and even when present they frequently cannot be correlated with the degree of urinary incontinence. Thus, marked urinary leakage may occur in patients with intact pelvic structures, whereas women who on exertion lose only a drop or two of urine may have a urethra and a bladder base that have obviously lost their normal attachments. Furthermore, a history of obstetric trauma may be absent, and it is well known that some women who have never borne children suffer from exertional incontinence. These facts suggest that the present ideas concerning the etiology of this condition require revision, and this need furnished the incentive for the present investigation.

A study of 140 women forms the basis of this report. Ninety-five patients had exertional incontinence, and 45 continent women who had had obstetric sequelae, such as cystocele, laceration of the perineum and prolapse of the uterus, were selected for control subjects. It will be seen from Table 1

TABLE 1 Comparative Data in Patients with Incontinence and in Control Patients

DATUM	PATIENTS WITH INCONTINENCE	CONTROL PATIENTS
Age (in years)		
Average	44	54
Youngest	24	21
Oldest	68	72
Parity		
Average	5	5
Extent	1-12	1-10
Bladder capacity (in cubic centimeters)		
Average	550	592
Largest	1150	950
Smallest	300	250

that the age, the obstetric experience and the bladder capacity of both groups were closely similar. The use of such a large control group was considered essential for the proper evaluation of the findings ordinarily associated with exertional incontinence.

The data obtained consisted of a detailed history, a complete physical examination, cystometry, cystourethroscopy, cystography and urethrography. At

the cystoscopic examination, particular attention was paid to the performance of the internal sphincter when closing and opening. In a few cases fluoroscopy of the bladder filled with a contrast medium (Diodrast) was done to study detrusor behavior. Infection of the urinary tract was ruled out by analysis and culture of a catheter specimen of urine.

Analysis of the data revealed no correlation between the number of deliveries, the difficulties of labor and the degree of incontinence, which was arbitrarily expressed on a basis of + to ++++. The percentile distribution of the various degrees of incontinence among the 95 patients studied is given in Table 2. The findings of the pelvic examina-

TABLE 2 Distribution of the Degree of Exertional Incontinence

DEGREE OF INCONTINENCE*	PERCENTAGE OF CASES
+	27
++	30
+++	26
++++	17

\* + = loss of a few drops of urine; ++++ loss of entire bladder contents; and ++ and +++ = intermediary degrees of incontinence.

tion could not be correlated with the severity of the incontinence. In many cases large cystoceles, uterine prolapse or extensive perineal tears were associated with only mild leakage of urine, whereas patients with marked incontinence had surprisingly good pelvic structures. The control group amply demonstrated that urinary continence need not be impaired by post-partum changes affecting the pelvis and perineum.

The cystometrograms, the cystograms and the cystoscopic findings were similar in both groups and revealed no specific criteria diagnostic of exertional incontinence. A properly functioning internal sphincter was demonstrable even in patients with marked incontinence.

The urethrograms revealed all sorts of urethral configurations without establishing an x-ray picture typical of exertional incontinence. The width and length of the urethra, its course in relation to the posterior surface of the symphysis pubis and its mobility had no demonstrable relation to urinary control (Figs 1-3).

DISCUSSION

The belief that exertional incontinence is caused by obstetric trauma is time-honored and has never been seriously questioned. This is understandable, because the majority of women who suffer from it have borne children and because some of them

\*From the Department of Urology, Beth Israel Hospital. Read at a meeting of the New England Section of the American Urological Association, Boston, April 26, 1945.  
†Assistant in urology, Harvard Medical School; instructor in urology, Tufts College Medical School; junior visiting urologist, Beth Israel Hospital.

## PYOGENIC LIVER ABSCESS

## Review of the Literature and Report of a Case Successfully Treated by Operation and Penicillin

LIEUTENANT COLONEL J. EDWARD FLYNN, M C, A U S \*

**P**YOGENIC abscesses of the liver have caused death in at least half the patients afflicted with this disease, the mortality having ranged from 50 per cent, in Eliason's<sup>1</sup> series, to 95 per cent, reported by Brütt.<sup>2</sup> Since chemotherapy has proved to be of great value in many diseases caused by pyogenic organisms, it seems logical that one of these drugs might be useful in cases of pyogenic liver abscess, and a case so treated is reported.

## ETIOLOGY

There are five ways in which pyogenic organisms invade the liver. First, they may travel through the portal vein from regions drained by it. Suppurative appendicitis, complicated by pylephlebitis, is one of the most frequent causes. In Ochsner's<sup>3</sup> collected series of 575 cases, appendicitis was the source in 197 (24 per cent). In the 47 cases of Ochsner's own series, however, appendicitis was the source in 11 per cent. The latter is probably a more accurate figure, because in a series of 231 cases reported by Baerensprung,<sup>4</sup> Rothenberg and Linder<sup>5</sup> and Keefer<sup>6</sup> appendicitis was the source in 15 per cent. Ulcerations of the stomach or bowel and diseases of the rectum, spleen and pancreas frequently cause hepatic abscess. In Ochsner's collected series, they constituted 10 per cent of all causes. Second, blood-borne infections may be transmitted through the hepatic artery. Osteomyelitis, furunculosis, ulcerative endocarditis, acute infections of the upper respiratory tract or pyemia from any source may be the cause. In Ochsner's collected series, 13 per cent were due to blood-borne infections. Third, there may be direct extension from a contiguous infection. A diseased gall bladder was the source in 14 per cent of Ochsner's collected series. Subphrenic abscess, empyema, nephritic or perinephritic abscesses and gastric and duodenal ulcers are less frequently the cause. Lastly, trauma may be the cause. This was so in 3 per cent of Ochsner's collected series. There may be a penetrating wound from a bullet or some other agent or a subcutaneous injury to the liver, producing traumatic changes in it and permitting the bacteria always present in this organ to grow.

Cases of pyogenic liver abscess in which the source cannot be determined form a relatively large group. In Ochsner's collected series, 17 per cent of the cases were of this type. In his own series of 47 cases, the incidence was 59 per cent. Such cases, Beaver<sup>7</sup> believes, are due to lesions draining into the portal vein that are so small that they cannot be localized clinically, whereas Rothenberg and

Linder<sup>5</sup> think that they are the result of hematogenous infections, secondary to small, inconspicuous distant foci. A case that falls into this group and in which pyogenic infection was due to nonhemolytic streptococci is presented below.

## BACTERIOLOGY

The organisms that cause pyogenic abscesses of the liver are generally sensitive to the sulfonamides or to penicillin. The organisms most frequently found are colon bacilli, streptococci, staphylococci or a combination of two or all of these. In Ochsner's collected series, the responsible organisms were colon bacilli in 31 per cent of the cases, streptococci in 21 per cent, staphylococci in 17 per cent, and two or more of these three in 17 per cent. Organisms that are rarely found are *Clostridium perfringens*, *Pseudomonas pyocyaneus*, *Eberthella typhosa*, *Leptothrix*,<sup>8</sup> *Streptothrix*,<sup>9</sup> *Salmonella*,<sup>10</sup> spirochetes<sup>11</sup> and gonococci.<sup>12</sup> Pus in pyogenic abscesses of the liver is frequently sterile. Rothenberg and Linder<sup>5</sup> found sterile pus in 46 per cent of their series, whereas Elsberg<sup>13</sup> reported it positive in 60 per cent of his series.

## PATHOGENESIS AND PATHOLOGY

It has been mentioned that pyogenic hepatic abscesses may develop by extension of infection through the portal vein, through hepatic arteries as metastatic abscesses, by direct extension from a nearby organ or by trauma. Munro<sup>14</sup> has stressed the lymphatic vessels, but most investigators believe that infection of the liver rarely if ever occurs by this route. The retroperitoneal route from the appendix to the liver has been mentioned by Korte,<sup>15</sup> Loison<sup>16</sup> and Walter-Sallis.<sup>17</sup>

The most frequent source is considered by most investigators to be suppurative appendicitis. The course of the infection is easy to follow as it proceeds from inflammation of the appendix to thrombophlebitis of the vessels in the appendix wall and thence to progressive phlebitis of the appendiceal, ileocecal, superior mesenteric and portal veins. A septic embolus can, however, be detached from the thrombus in the appendiceal region. Most hepatic abscesses that follow appendicitis are multiple and involve the right lobe of the liver. The existence of two currents of blood in the portal vein, one from the superior mesenteric vein, which leads to the right lobe of the liver, and one from the inferior mesenteric and splenic veins, which lead to the left lobe, has been demonstrated by Sérégé,<sup>18</sup> Glénard,<sup>19</sup> Bartlett, Corper and Long<sup>20</sup> and Copher and Dick.<sup>21</sup>

From the pathological standpoint, the first con-

\*Instructor in surgery Tufts College Medical School, and assistant to various surgeons. Second Surgical Service Boston City Hospital (on leave of absence).

importance to urinary continence. More than two thirds of the female urethra can be safely excised — as it usually is for carcinoma of the urethra — without causing loss of urinary control,<sup>5, 6</sup> showing that the normal mechanism responsible for continence does not reside in the distal two thirds of the urethra.

The only significant urethral sphincter, according to recent investigations, consists of the fibers of the detrusor at the bladder outlet or neck.<sup>7-10</sup> This sphincter is an integral part of the detrusor, and its behavior is entirely dependent on it, as was shown by the studies of Denny-Brown and Robertson<sup>11, 12</sup>. These authors have clearly demonstrated that no independent relaxation of the internal vesical sphincter can occur without corresponding contraction of the detrusor. The bladder neck therefore cannot open even partially unless the detrusor contracts simultaneously. For the escape of urine, to be interrupted, detrusor contractions must be inhibited.

The function of the detrusor in exertional incontinence was investigated in a series of 7 patients. The bladder was filled with Diodrast, and its behavior was observed under the fluoroscope. When micturition was initiated, contraction of the bladder dome was first seen. This was followed by straightening of the lateral walls and centripetal contraction of the entire bladder muscle. When requested to inhibit the urinary stream, control subjects were promptly able to relax the detrusor. Patients with exertional incontinence, on the other hand, invariably accomplished this only with difficulty. The detrusor muscle continued to contract for a variable time after the initial voluntary effort to stop urination, this interval being commensurate with the degree of incontinence. Patients with marked incontinence either inhibited the bladder contractions late during urination or proceeded to complete the micturition.

These observations, although based on the study of a small series of cases, nevertheless emphasize the importance of proper detrusor function in normal micturition and in the presence of urinary incontinence. They suggest that exertional incontinence is due to an acquired irritability of the detrusor that permits minor stimuli, such as are set off by coughing or sneezing, to produce detrusor contractions, with corresponding relaxation of the internal sphincter and urinary leakage. If this assumption is correct, the source of the trouble in exertional incontinence is not in the urethra, its sphincters or supports but in the bladder muscle itself and its internal sphincter. The normal mechanism, which keeps the detrusor relaxed until micturition is initiated or which relaxes it at will when the urinary stream is to be inhibited, is disturbed. The cause of such an acquired detrusor dysfunction, however, must at present be regarded as unknown. In pre-

vious reports it was shown that the bladder muscle can be strikingly affected by hormones.<sup>13, 14</sup> The hormonal changes associated with pregnancy and the puerperium profoundly alter bladder capacity and tonus. Hormonal changes occur also at the menopause, when many women first develop exertional incontinence. The precise relation between female hormones and this type of urinary leakage, however, is yet to be established.

The concept of exertional incontinence as a functional bladder disturbance undermines the basis on which the present methods of surgical treatment rest. The various plication operations and the procedures involving the use of fascial slings around the urethra do not attack the problem at its root. By their fixation of the bladder neck they do, however, make it difficult for the internal sphincter to open easily in response to detrusor contractions. It is probably for this reason that overfixation of the bladder neck has often led to inability to void, whereas insufficient fixation has produced only fleeting relief from incontinence.

#### SUMMARY

No specific urethral lesion was found in a study of 95 patients with exertional incontinence, as compared with 45 control subjects.

The belief that obstetric trauma causes exertional incontinence is critically reviewed, and the conclusion is reached that it is not an etiologic factor.

Evidence is presented that exertional incontinence is due to an acquired dysfunction of the detrusor rather than to anatomic defects.

520 Beacon Street

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the anteroposterior view and of the posterior costophrenic angle in the lateral view. Miles<sup>44</sup> showed that a gastrointestinal series in the presence of an abscess in the left lobe of the liver presents a deformity in which the lesser curvature of the stomach assumes a crescentic shape and the cardia and duodenal cap are displaced.

### DIFFERENTIAL DIAGNOSIS

It is often possible to differentiate multiple and single abscesses of the liver. The former have an acute, sudden onset and are usually secondary to pyelephlebitis and suppurative appendicitis, whereas single pyogenic abscesses generally have an insidious onset and in many cases it is impossible to determine the source. Fever, chills and leukocytosis are more prominent with multiple than with single abscesses. Amebic abscesses of the liver usually have an insidious onset. The temperature is only slightly increased, chills rarely occur, and *Endamoeba histolytica* may be found in the stools.

Intrahepatic — toxic or infectious — jaundice is accompanied by damage to the parenchymal liver tissue. The van den Bergh reaction is generally direct.<sup>45</sup> There may be no pain and little or no fever, and the onset is usually insidious.

Acute cholecystitis and empyema of the gall bladder must frequently be considered. In cases in which there are definite pathologic changes in the right upper quadrant of the abdomen, a conscientious perusal of the past history may be a great aid in establishing a diagnosis of acute cholecystitis. If there have been repeated attacks after the ingestion of fatty or fried foods or repeated attacks of colic of the type associated with gallstones, it is reasonable to assume that the gall bladder is the seat of the trouble. Nausea and vomiting are frequent. Definite localized tenderness and rigidity of the right rectus muscle in the upper quadrant of the abdomen can be demonstrated.

Exploratory aspiration of the liver for detection of pus in pyogenic hepatic abscess is a dangerous procedure and should be condemned because of the danger of contaminating the pleura or peritoneum. This condition can be readily diagnosed by other methods.

### PROGNOSIS

In the past, the prognosis with hepatic abscess has been extremely poor. Dieulafoy<sup>46</sup> in 1898 held that hepatic abscess following appendicitis was invariably fatal. Thompson<sup>47</sup> and Gerster<sup>48</sup> a few years later wrote of the seriousness of the condition. In 1914, Petrén<sup>48</sup> reported a mortality of 93 per cent. Later, Brütt<sup>2</sup> recorded one of 95 per cent, and in 1932 Otschkin<sup>49</sup> gave one of 80 per cent. Ochsner<sup>3</sup> clearly demonstrated that the mortality is much greater with multiple abscesses (95 per cent) than with single ones (37 per cent).

Obviously the prognosis in cases of pyogenic

hepatic abscess has been extremely grave, and it is of interest that the mortality rate has changed little during the last fifty years. With chemotherapy, however, it should be greatly reduced.

### TREATMENT

As a prophylactic measure in cases of appendicitis with a history of preoperative chills, the appendiceal ileocolic, superior mesenteric and portal veins should be examined during operation, as suggested by Melchior<sup>50</sup> and Thalheimer.<sup>50</sup> This may reveal a thrombosis, prompt treatment of which may prevent the development of hepatic pyogenic abscess. It seems likely that chemotherapy will also prove to have great prophylactic value.

The treatment of pyelephlebitis is surgical. Melchior<sup>51</sup> reported 13 cases in which ligation of the ileocolic vein was performed. Eight of these patients had ligation at the time of appendectomy or drainage, and none died. In the other 5 cases ligation was performed after the primary operation, and 1 patient died. In 1935 Stewart-Wallace<sup>52</sup> reported 15 cases in which primary ligation was performed. Two patients died from peritonitis. He also reported 6 cases in which the superior mesenteric vein was ligated. 4 patients recovered. Stewart-Wallace concluded that it is possible to ligate the superior mesenteric vein at or below the levels of the transverse mesocolon and the third part of the duodenum without the development of bowel necrosis.

Incision and drainage is the proper treatment of solitary pyogenic hepatic abscess. Ochsner<sup>3</sup> stresses the importance of using the type of drainage that avoids the possibility of contamination of the pleura or peritoneum.

An extraperitoneal anterior or posterior approach may be made, depending on the location of the abscess. With an abscess on the anterior or antero-inferior surface of the liver, a procedure similar to that described by Clairmont and Meyer<sup>53</sup> for drainage of subphrenic abscesses should be used. A skin incision is made anteriorly just beneath and parallel to the costal margin. The external and internal oblique muscles and transversalis fascia are cut. The parietal peritoneum is carefully dissected from the inferior surface of the diaphragm. If the abscess is reached it is drained extraperitoneally at this stage. If it is not reached extraperitoneally, the visceral and parietal surfaces of the peritoneum are made to adhere by packing the area with gauze impregnated with some irritative substance, and drainage is later performed through this area.

If there is no sign of localization of the abscess in the anterior abdominal region, the retroperitoneal approach described by Ochsner<sup>3</sup>,<sup>54</sup> is used. A skin incision is made directly over the twelfth rib, which is resected subperiosteally. A transverse incision is made through the resected bed of the

sideration is the pylephlebitis. The infection in most cases invades the vein from without, the phlebitis being preceded by inflammation in the wall of the appendix. The inflammatory process may extend along the course of the vein, so that phlebitis has every facility for extension. The wall of the vein is infiltrated with leukocytes. Thrombosis rapidly occurs. The clot softens and mingles with the pus from the vessel wall. The inflammatory process may weaken the wall, with subsequent dilation of the vein, which may perforate, permitting the escape of blood and pus into the hepatic tissue. In other cases the inflammation is carried to the wall of the vein, with the early formation of a septic thrombus. Septic emboli may be carried through the portal system and produce hepatic abscesses.

Grossly the liver is enlarged. The abscesses are usually multiple, they vary in diameter from 0.5 mm to 10 cm and are generally confined to some particular section of the liver, the right lobe being involved oftener than the left. The multiple abscesses give the liver a mottled appearance. Small abscesses may coalesce, forming larger ones, and large solitary abscesses may become chronic. Beaver<sup>7</sup> has described granulomatous abscesses of the liver.

The lung or pleural cavity may be involved by a spread of infection through the diaphragm, or rarely by a septic embolus. Usually a solitary abscess in the right lobe of the liver is the cause of pleuropulmonary complications. In Ochsner's<sup>3</sup> collected series, pneumonia was a complication in 11 per cent of the cases, lung abscesses were present in 9 per cent, and empyema was found in 4 per cent.

Peritonitis may occur as the result of rupture of the abscess into the peritoneal cavity or following transperitoneal drainage of the abscess. In Keefe's<sup>6</sup> series, peritonitis complicated liver abscess in 8 per cent of the cases. Subphrenic abscess was found as a complication in 6 per cent.

If the hepatic abscesses are due to pyemia, abscesses may also be found in the lungs, kidneys, spleen and brain.

Unusual complications have been reported by some investigators. Rupture of a hepatic abscess into the pericardium has been reported by Keefer<sup>6</sup> and Azar,<sup>22</sup> into the abdominal wall, by Huard et al.,<sup>23</sup> into the vena cava, by McKnight<sup>24</sup> and into the thoracic duct by Nieweg.<sup>25</sup> The occurrence of a pulmonary infarct has been cited by Keefer.<sup>6</sup>

#### SYMPTOMS AND SIGNS

The usual systemic symptoms are fever, chills, pain and profuse sweating. Less often malaise, anorexia, loss of weight, weakness, nausea and vomiting occur. Fever may be continuous, intermittent or remittent. With acute suppurative appendicitis complicated by pylephlebitis and multiple abscesses of the liver, fever is of the so-

called "picket-fence" type and is generally accompanied by daily chills. Rothenberg and Linder<sup>1</sup> observed that daily chills occurred frequently with multiple hepatic abscesses but were rare with a single abscess. As far back as 1897 Bryant<sup>26</sup> called attention to the significance of chills and fever during the course of appendicitis. Brown,<sup>27</sup> Gerster,<sup>28</sup> Babler,<sup>29</sup> Thalhimer,<sup>30</sup> Ehason,<sup>1</sup> Ochsner et al.<sup>31</sup> and others have emphasized this point.

Pain is felt in the right upper quadrant of the abdomen and is usually constant. In Ochsner's collected series, pain was present in 91 per cent of the cases. Dixon and Murphy<sup>32</sup> observed radiation of pain from the right hypochondrium to the right shoulder, probably owing to irritation of the phrenic nerve. Rothenberg and Linder<sup>1</sup> believe that irritation of the phrenic nerve seldom occurs, but state that over one third of patients complain of pain in the right lower chest on inspiration, indicating a diaphragmatic pleurisy. Intercostal pain may occur, as described by Rothenberg and Linder, Ehason<sup>1</sup> and Alessandri.<sup>33</sup> Weakness, anorexia and loss of weight are frequent. Nausea and vomiting seldom occur and were present in less than one third of Ochsner's collected cases.

Tenderness over the liver area and hepatic enlargement are frequent local signs. Rothenberg and Linder<sup>1</sup> found tenderness in all their cases and hepatic enlargement in 92 per cent.

Jaundice occurs infrequently and is usually a late serious sign. Jaundice occurred in 8 per cent of Rothenberg and Linder's cases and in 25 per cent of Ochsner's collected series. Ascites is rare.

#### LABORATORY DATA

Leukocytosis, with an increase in polymorphonuclear leukocytes, is almost invariably present. The contrast between the moderate leukocytosis accompanying amebic abscess and the greater leukocytosis of pyogenic hepatic abscess has been mentioned by Rogers,<sup>34</sup> Manson-Bahr and Willoughby<sup>35</sup> and Ochsner and DeBakey.<sup>36</sup> The leukocytosis in acute cases is about twice as high as that in chronic cases.

Urinalysis is usually negative, but with jaundice bile is found in the urine, and with marked toxemia there is albuminuria.

Ochsner<sup>3</sup> believes that roentgenography is one of the most significant and reliable aids in the diagnosis of liver abscess. The elevation and immobility of the diaphragm, usually on the right, as seen by x-ray are of high diagnostic value according to Pancoast,<sup>37</sup> Dickinson,<sup>38</sup> Love<sup>39</sup> and Oschner.<sup>4</sup> Granger<sup>40</sup> and Ochsner and DeBakey<sup>36, 41-43</sup> have observed that in subphrenic abscess complicating liver abscess there is obliteration of the cardiophrenic angle in the anteroposterior view and of the anterior costophrenic angle in the lateral view, whereas in subphrenic abscess due to other causes there is obliteration of the costophrenic angle in

A case of multiple pyogenic hepatic abscesses is presented. This case may be the forerunner of many others in which the patients survive when treated properly with penicillin or sulfadiazine. Etiologically, this patient belonged to the so-called "idiopathic group," in which the source of the infection cannot be determined. The organism was a nonhemolytic streptococcus sensitive to penicillin. Recovery followed penicillin therapy of three weeks' duration.

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twelfth rib and the serratus posterior inferior muscle at the level of the spinous process of the first lumbar vertebra. The pleura at the costophrenic angle never extends below the spinous process of the first lumbar vertebra. The retroperitoneal space is entered between the upper pole of the kidney and the inferior surface of the liver. The parietal peritoneum is dissected from the undersurface of the diaphragm and the liver abscess is drained extraperitoneally. The importance of an extraperitoneal approach is stressed by Ochsner,<sup>3</sup> who cites a mortality of 33 per cent with an extraperitoneal approach, one of 67 per cent with a transpleural approach and one of 73 per cent with a transperitoneal approach.

Chemotherapy should play a significant role in the decrease in mortality with multiple pyogenic abscesses of the liver. If operation is performed it is important to culture the organisms and test their sensitivity to penicillin and to sulfadiazine.

\* \* \*

A case of multiple pyogenic abscesses of the liver, due to nonhemolytic streptococci, with no demonstrable focus, is presented below. The organism was sensitive to penicillin. The patient made a complete recovery. No similar case can be found in the literature.

#### CASE REPORT

The patient was a 23-year-old American soldier, born in Italy. The first symptom was a dull pain in the right upper quadrant of the abdomen, which lasted for 30 minutes. The pain recurred in 2 days, and the patient was admitted to a station hospital. The pain was intermittent and dull and persisted for 3 days. On the 3rd day after the onset of symptoms, the patient became jaundiced. On the 8th day, chills and a temperature of 101°F developed, persisting for 3 days. On the 14th day, a temperature of 101°F and chills recurred and lasted for 2 days. On the 21st day, pain recurred in the right upper quadrant of the abdomen. The patient vomited twice and had chills and a temperature of 102°F. Pain persisted for 1 day. On the 26th day, pain, fever, chills and vomiting recurred and lasted for 1 day. Jaundice and clay-colored stools persisted for 3 weeks. A diagnosis of catarrhal jaundice was made. After 5 weeks the patient was transferred to a convalescent hospital.

The patient was symptom-free for 3 days while in the convalescent hospital. On the 41st day after the onset of symptoms, the fifth attack of pain occurred. Pain was felt in the right and left upper quadrants of the abdomen and radiated to the right shoulder. The patient vomited once and jaundice recurred for the second time. There were chills and a temperature of 103°F. On physical examination there was tenderness and spasm over the right upper quadrant of the abdomen. The white-cell count was 16,500. Pain and jaundice persisted for 1 week.

The patient was symptom-free for the next 10 days. Pain in the right upper quadrant recurred for the sixth time, and jaundice for the third time. The liver edge was palpated 2 fingerbreadths below the costal margin. There were tenderness and spasm in the right upper quadrant. A diagnosis of probable empyema of the gall bladder was made, and the patient was prepared for surgery.

Operation was performed under spinal anesthesia, and the abdomen was opened. The liver was enlarged, with many white areas varying from 1 mm to 5 cm in diameter. A large, fluctuant mass measuring 5 cm in diameter was seen. Pus was aspirated from the abscess and a biopsy of the liver edge was performed. The gall bladder was distended, and grayish fluid was aspirated from it. The common duct was not dilated. A cholecystostomy was performed, and a

cigarette drain was inserted in the right subhepatic region. The wound was closed in layers except for the drain. A culture of pus aspirated from the abscess at operation showed microaerophilic nonhemolytic streptococci. The organisms were sensitive to penicillin, the zone of inhibition being 18 mm in diameter.

The pathological report was as follows: The gross specimen consists of a section of the liver measuring 5 by 3 by 2 cm. A gray area of pin-point size is seen in the yellow gray surface. Lobulation cannot be made out.

Microscopical examination shows that about half the normal architecture has been destroyed by an acute inflammatory process in and about the bile ducts, with necrosis of the adjacent liver cords and abscess formation. In addition to infiltration by polymorphonuclear leukocytes, there are a considerable number of eosinophils in the inflammatory reaction. There is hyperplasia of duct epithelium and early fibroplastic replacement of destroyed parenchyma. Diagnosis: acute cholangitis, with abscess formation.

Urinalysis was negative except during the periods when the patient was having pain and jaundice, when bile and albumin were found. On the day of operation the urine was amber, the specific gravity was 1.010, and there was a ++ test for albumin. There was an acid reaction, and no sugar and the test for bile was strongly positive.

The white-cell count during the acute attacks ranged from 10,500 to 21,000, with 79 per cent segmented neutrophils, 12 per cent lymphocytes, 6 per cent stab forms, 2 per cent monocytes and 1 per cent eosinophils. The red-cell count during the acute attacks ran about 3,100,000, with a hemoglobin of 78 per cent. Multiple smears showed no malarial parasites.

The icteric index during the phases of jaundice ranged from 11 to 43. The prothrombin time on the day before operation was 4 minutes for the patient and 3 minutes for the control. Three weeks postoperatively it was 16 and 6½ minutes, respectively, and 5 weeks postoperatively it was 5.5 and 4 minutes, respectively.

Three weeks preoperatively, the van den Bergh reaction was indirect, with 0.3 mg per 100 cc. Three weeks postoperatively, it was again indirect, with 2.4 mg and 4 weeks postoperatively it was indirect, with 2.1 mg.

Serologic tests for syphilis, tularemia, undulant fever and typhoid fever were negative. Dark-field examination of the blood was negative. Multiple stool examinations were negative for bile, occult blood, parasites and ova.

Blood cultures taken 4 weeks and 1 week preoperatively showed no growth. Culture of bile from the cholecystostomy showed nonhemolytic streptococci, nonhemolytic staphylococci and gram-negative rods not of the enteric group. Many x-ray films of the chest and abdomen showed no abnormality.

An electrocardiogram taken 3 weeks preoperatively showed sinus tachycardia. Low amplitude and low T waves were observed, findings similar to those in coronary disease, early pericarditis and systemic infection of long standing.

The patient was given 20,000 units of penicillin every 3 hours for 3 weeks postoperatively. Intravenous therapy was given for 4 days, and oral feeding was then begun. Five days postoperatively the temperature became normal and remained so. The cholecystostomy tube fell out on the 5th day. The wound was entirely healed 16 days after operation, when the patient was permitted out of bed. He was discharged 6 weeks after operation. A check-up examination 5 months after operation was negative. The patient will be followed indefinitely, especially for signs of biliary cirrhosis.

One and a half years postoperatively, the patient reported that he was well.

#### SUMMARY

Pyogenic hepatic abscess has caused a mortality of 50 to 95 per cent in patients afflicted with this disease.

Since the infection is usually caused by an organism that is sensitive to the sulfonamides or penicillin, chemotherapy should cause a great decrease in the mortality, but early diagnosis and proper operative procedures are also important.

730 consecutive cases of acute appendicitis admitted to St Thomas's Hospital in London. They believe that all patients save those presenting a palpable mass should be operated on soon after admission. They recognize that children are exceptions to this rule, and advise modification of this dictum in pregnancy and in the aged. Eight of the 21 fatalities in their series were in patients over sixty years of age.

The above two reports are in accord with the findings of Rogers and Faxon,<sup>8</sup> who studied the appendicitis data from the Massachusetts General Hospital. The rationale of not spreading a localized inflammatory mass by immediate appendectomy is obvious. The abscess can be drained if it develops, and the appendix can be safely removed a few weeks later. Better preoperative and postoperative management has reduced the morbidity and mortality in cases with spreading peritonitis. There still remains an occasional case of this sort in which the patient is too ill for immediate surgery.

Sewell<sup>9</sup> reports on two groups of patients from the same community and attributes a marked improvement in results largely to the use of sulfonamides. He reports the loss of 1 patient in the last consecutive 300 cases of appendicitis treated. Of these, the appendix was gangrenous in 31 cases and was perforated at the time of operation in 33. Sewell believes that the elimination of drains and the change from catgut to fine silk have also contributed to the reduction of intestinal obstruction and wound infection.

Obstructive appendicitis is discussed by Bowen.<sup>10</sup> He reviews Wilkie's<sup>11</sup> original concept of this type of appendicitis. It appears that about 14 per cent of all Bowen's cases of acute appendicitis were of the obstructive type. In 38 cases studied for the cause of this condition, a stercorolith was present in 21, kinks and bands in 4, and stenosis in 1, whereas in 12 cases the only etiologic factor seemed to be spasm. Inasmuch as fever develops late and leukocytosis is always present early, there is little excuse for not recognizing this entity before perforation occurs. Since this type of appendicitis accounts for most of the cases of associated peritonitis due to early rupture of the appendix, and therefore for most of the deaths in appendicitis, it is all the more important to have this possibility in mind when acute abdominal symptoms occur.

Knox<sup>12</sup> reviews the literature on primary lymphosarcoma of the appendix and cites another case, making a total of 24 cases so far reported. Of twelve and a half thousand appendectomies performed at St. Luke's Hospital, New York City, since 1910, this was the only case in which such a diagnosis was made.

#### BILIARY SYSTEM

From the literature since 1900 Dixon and Lichtman<sup>13</sup> have collected 50 cases of congenital absence

of the gall bladder, and have added 10 cases from the records of the Mayo Clinic. Fifty-eight per cent of these 60 patients had symptoms of cholelithiasis, 48 per cent had jaundice, and 27 per cent had gallstones in the ducts. Of the patients beyond the age of forty-five, 73 per cent had developed symptoms referable to the biliary tract.

Two case reports of papilloma of the gall bladder are presented by Greenwald.<sup>14</sup> Such patients have the symptoms found in the more frequent pathologic states of the biliary system. The diagnosis is made by roentgen-ray examination after administration of the usual dye for cholecystograms. Palpation of the gall bladder does not reveal the lesion, because the papillomas are soft. Cholecystectomy is recommended. The possibility of malignant degeneration is discussed.

Smith<sup>15</sup> has reported the experience of the Presbyterian Hospital, New York City, with acute cholecystitis for a ten-year period ending in 1941. He concludes that operation should be undertaken as soon as the patient is properly prepared and optimum operating-room facilities are available. The operative mortality increased with the duration of the acute process. Two hundred and twenty-three patients had cholecystectomy, with 8 deaths, a mortality of 4 per cent. Of 103 who had cholecystostomy, 12 died. There was an overall mortality of 7 per cent, which corresponds closely to the mortality of a similar group of patients at the Massachusetts General Hospital.<sup>16</sup>

An excellent discussion on the pitfalls in cholecystectomy has been presented by Simon.<sup>17</sup> Schematic drawings and some photographs taken at operation illustrate the numerous anomalies that may be found in the ducts and blood vessels of the gall-bladder region. The author believes that these variations account for many of the catastrophes occurring during cholecystectomy. He thinks that the surgeon obtains a better opportunity for recognizing the anomalous as well as the normal structures by making the dissection from the fundus of the gall bladder toward the ducts.

Colp<sup>18</sup> has reported the results of repair in 5 cases of traumatic stricture of the hepatic ducts. He used a fenestrated tube placed well up in the right hepatic duct and led into the duodenum. In 1 patient, the tube was brought out through the stomach wall and failed because it had to be removed on the eleventh day after a gastric fistula had developed. One patient was well for four and a half years, 1 for one and a half years, and 1 for two months. The remaining 2 patients have had recurrent chills and fever.

Peterson and Cole<sup>19</sup> treated 3 patients for biliary obstruction due to sclerosing pancreatitis. All had different types of operative procedures to restore the bile flow to the gastrointestinal tract. These authors prefer the Roux type of operation, and have tried to make valvelike infoldings in the segment

## MEDICAL PROGRESS

### ABDOMINAL SURGERY

ARTHUR W ALLEN, M D\*

BOSTON

MANY contributions relating to surgical lesions of the abdomen have been reviewed during the past year. It is impossible to refer to all of them in this report, but a large proportion of the most significant are mentioned, and comments are made according to their relation to experience at the Massachusetts General Hospital.

#### ANESTHESIA

Lemmon and Hager<sup>1</sup> have reported on continuous spinal anesthesia in 2000 cases. They had no deaths and few complications from this method. Of these patients, 3.1 per cent had post-anesthesia headache, 3.3 per cent had urinary retention, and 2.3 per cent had pulmonary complications. Four and one tenth per cent of the patients died from causes unrelated to the anesthesia in an average of about six days. The surgical procedures were mainly abdominal and pelvic but included forty-eight thoracic operations.

This experience is in accord with that of Arrowood and Foldes,<sup>2</sup> who have modified Lemmon's method by a continuous intrathecal novocain drip. The patient is often kept asleep by small doses of Pentothal Sodium given intravenously as an adjunct to the spinal novocain. In this modification the relaxation of the abdominal muscles is continuous and completely satisfactory to the surgeon.

#### HERNIA

Singleton and Stehouwer<sup>3</sup> report their experience with the fascia-patch method of hernia repair in 129 cases, supplementing a preliminary report on 44 patients made in 1916. They remove a semilunar-shaped piece of fascia lata and suture it to the structures bordering the inguinal canal. They have had recurrences in 3 per cent of indirect, 11 per cent of direct and 18 per cent of ventral and incisional hernias — an average rate of 11 per cent. They point out that 62 per cent of their cases had had previous repairs and that most of these were described as difficult.

Mair<sup>4</sup> makes a preliminary report on the use of a whole-thickness skin transplant in the repair of hernia. The region is prepared with soap and water for three successive days before operation. The incision over the hernia is elliptical, so that a piece of skin measuring 2.5 by 5.0 cm. can be obtained and

placed in normal salt solution. The cord is elevated, the sac is attended to in the usual manner, and the floor of the canal is narrowed by sutures. The graft is then freed of fat, cut off square at both ends and sutured under the cord to the rectus fascia, Poupart's ligament and the conjoined tendon. The outer end of the graft is split and sutured around the cord to make a new internal ring. Cultures from the graft have occasionally yielded *Staphylococcus albus*. In spite of this, there were only 2 cases of wound infection in 88 cases, and apparently neither of these caused sloughing of the graft. Mair's experimental work on rabbits and the re-exploration of the region of the graft three months later for some reason in one of his patients enables him to state that skin under these circumstances changes its character to a white fibrous structure. His patients were allowed up on the twentieth postoperative day.

Skinner and Duncan<sup>5</sup> report on one hundred and twenty-six recurrent hernias repaired by them, with four failures, which were due to incorrect selection of procedure, infection, cough and poor tissues. They encountered five types of recurrence, namely, at the internal ring, near the pubis, at the midportion of the canal, as a femoral hernia overlooked at the first operation and as a general bulge below the repair.

Many reports substantiate our belief that when hernias are recurrent or large or the tissues are poor, the fascial-strip method of Gallie and LeMeasurer is the simplest procedure and offers the best opportunity for cure.

#### APPENDICITIS

Ochsner and Johnston<sup>6</sup> have made a comparative study of the records on patients admitted to the Charity Hospital in New Orleans with appendiceal peritonitis in the years 1933 and 1943. The percentage of ruptured appendices was reduced, but the percentage of cases having received preadmission catharsis remained unchanged. There was a lower mortality and a lower morbidity rate in the more recent group of cases. These authors give credit to chemotherapy, the use of blood and plasma, more logical fluid replacement and delayed wound closure for their better results. They stress the use of delayed operation only in the presence of a palpable mass.

This is in accord with the viewpoint of McPherson and Kinmonth,<sup>7</sup> who have analyzed the records of

\*Lecturer in surgery, Harvard Medical School, chief, East Surgical Service, Massachusetts General Hospital.

730 consecutive cases of acute appendicitis admitted to St Thomas's Hospital in London. They believe that all patients save those presenting a palpable mass should be operated on soon after admission. They recognize that children are exceptions to this rule, and advise modification of this dictum in pregnancy and in the aged. Eight of the 21 fatalities in their series were in patients over sixty years of age.

The above two reports are in accord with the findings of Rogers and Faxon,<sup>8</sup> who studied the appendicitis data from the Massachusetts General Hospital. The rationale of not spreading a localized inflammatory mass by immediate appendectomy is obvious. The abscess can be drained if it develops, and the appendix can be safely removed a few weeks later. Better preoperative and postoperative management has reduced the morbidity and mortality in cases with spreading peritonitis. There still remains an occasional case of this sort in which the patient is too ill for immediate surgery.

Sewell<sup>9</sup> reports on two groups of patients from the same community and attributes a marked improvement in results largely to the use of sulfonamides. He reports the loss of 1 patient in the last consecutive 300 cases of appendicitis treated. Of these, the appendix was gangrenous in 31 cases and was perforated at the time of operation in 33. Sewell believes that the elimination of drains and the change from catgut to fine silk have also contributed to the reduction of intestinal obstruction and wound infection.

Obstructive appendicitis is discussed by Bowen.<sup>10</sup> He reviews Wilkie's<sup>11</sup> original concept of this type of appendicitis. It appears that about 14 per cent of all Bowen's cases of acute appendicitis were of the obstructive type. In 38 cases studied for the cause of this condition, a stercorolith was present in 21, kinks and bands in 4, and stenosis in 1, whereas in 12 cases the only etiologic factor seemed to be spasm. Inasmuch as fever develops late and leukocytosis is always present early, there is little excuse for not recognizing this entity before perforation occurs. Since this type of appendicitis accounts for most of the cases of associated peritonitis due to early rupture of the appendix, and therefore for most of the deaths in appendicitis, it is all the more important to have this possibility in mind when acute abdominal symptoms occur.

Knox<sup>12</sup> reviews the literature on primary lymphosarcoma of the appendix and cites another case, making a total of 24 cases so far reported. Of twelve and a half thousand appendectomies performed at St Luke's Hospital, New York City, since 1910, this was the only case in which such a diagnosis was made.

#### BILIARY SYSTEM

From the literature since 1900 Dixon and Lichtman<sup>13</sup> have collected 50 cases of congenital absence

of the gall bladder, and have added 10 cases from the records of the Mayo Clinic. Fifty-eight per cent of these 60 patients had symptoms of cholelithic disease, 48 per cent had jaundice, and 27 per cent had gallstones in the ducts. Of the patients beyond the age of forty-five, 73 per cent had developed symptoms referable to the biliary tract.

Two case reports of papilloma of the gall bladder are presented by Greenwald.<sup>14</sup> Such patients have the symptoms found in the more frequent pathologic states of the biliary system. The diagnosis is made by roentgen-ray examination after administration of the usual dye for cholecystograms. Palpation of the gall bladder does not reveal the lesion, because the papillomas are soft. Cholecystectomy is recommended. The possibility of malignant degeneration is discussed.

Smith<sup>15</sup> has reported the experience of the Presbyterian Hospital, New York City, with acute cholecystitis for a ten-year period ending, in 1941. He concludes that operation should be undertaken as soon as the patient is properly prepared and optimum operating-room facilities are available. The operative mortality increased with the duration of the acute process. Two hundred and twenty-three patients had cholecystectomy, with 8 deaths, a mortality of 4 per cent. Of 103 who had cholecystostomy, 12 died. There was an overall mortality of 7 per cent, which corresponds closely to the mortality of a similar group of patients at the Massachusetts General Hospital.<sup>16</sup>

An excellent discussion on the pitfalls in cholecystectomy has been presented by Simon.<sup>17</sup> Schematic drawings and some photographs taken at operation illustrate the numerous anomalies that may be found in the ducts and blood vessels of the gall-bladder region. The author believes that these variations account for many of the catastrophes occurring during cholecystectomy. He thinks that the surgeon obtains a better opportunity for recognizing the anomalous as well as the normal structures by making the dissection from the fundus of the gall bladder toward the ducts.

Colp<sup>18</sup> has reported the results of repair in 5 cases of traumatic stricture of the hepatic ducts. He used a fenestrated tube placed well up in the right hepatic duct and led into the duodenum. In 1 patient, the tube was brought out through the stomach wall and failed because it had to be removed on the eleventh day after a gastric fistula had developed. One patient was well for four and a half years, 1 for one and a half years, and 1 for two months. The remaining 2 patients have had recurrent chills and fever.

Peterson and Cole<sup>19</sup> treated 3 patients for biliary obstruction due to sclerosing pancreatitis. All had different types of operative procedures to restore the bile flow to the gastrointestinal tract. These authors prefer the Roux type of operation, and have tried to make valvelike infoldings in the segment

of bowel leading away from the liver in an effort to prevent regurgitation of gastrointestinal contents into the hepatic system

I<sup>20</sup> have described in detail a method of re-establishing continuity between the hepatic ducts and the intestine, based on the Roux principle. Fourteen patients have been operated on by this method so far. In those whose ducts are large and the obstruction is due to pancreatic disorders, the method is simple and easily accomplished. In those who have suffered trauma to the ducts, an end-to-end suture should be made if enough of the duct is available after excising the stricture. Often, however, little of the common hepatic duct is left, and in these cases we believe that our method is particularly applicable. The anastomosis should be made over a removable tube. The chief difficulties have arisen when the tube has come out of the duct too soon. We believe that it should be left in place for three months, in the hope that a permanent communication can be established and the supporting tube eliminated.

Lahey<sup>21</sup> has written an excellent editorial on the subject of injuries to the common and hepatic bile ducts. He stresses the importance of early recognition of the injury and the need for repair by surgeons experienced in this field.

#### STOMACH

The relation between achlorhydria, polyposis and ultimate carcinoma of the stomach has been synchronized by Castle.<sup>22</sup> Olson and Heck<sup>23</sup> studied the data available at the Mayo Clinic and found that only 2 of 63 patients with untreated pernicious anemia developed cancer of the stomach in an average of two years. Thirty-one patients were treated for their anemia, and 6 of these developed cancer of the stomach in an average of five and a half years. Thus, it appears that, with a better life expectancy from pernicious anemia, the ratio of cancer of the stomach in such cases will be much higher than it is in normal persons.

Bisgard and Overmiller<sup>24</sup> believe that radical resection is indicated in perforated cancer of the stomach. They have collected from the literature 100 cases in which the perforation was closed or tamponaded by omentum, 76 of these patients died. In fifteen resections for this complication, there were 2 fatalities. These authors believe that 50 per cent of the cancers of the stomach that perforate are resectable.

Engel<sup>25</sup> advocates the fashioning of a gastric pouch following total gastrectomy for cancer. Since some patients complain of not being able to take food in adequate quantities following total gastrectomy, his concept seems logical. The pouch is constructed by making a long anastomosis between the two limbs of the jejunum, starting just below the esophagojejunostomy. It has long been recognized that a liberal enteroenterostomy between the

afferent and efferent jejunal limbs is advantageous. The larger pouch may well be an asset and should be tried.

Gastrojejunocolic fistula has been discussed by Marshall.<sup>26</sup> He advocates a preliminary ileosigmoidostomy to eliminate regurgitation of intestinal contents into the stomach. Later the fistula is resected, preferably with the usual radical stomach resection for duodenal ulcer. In 14 patients, there was 1 death following the first stage.

Ransom<sup>27</sup> reports on 14 cases of gastrojejunocolic fistula treated as follows. Ten patients had the fistulas resected without radical operation for the original duodenal ulcer, with 1 death. There were good results in 4 cases and recurrence of duodenal ulcer symptoms in 5 cases, in 3 of which radical subtotal gastrectomy was performed. Four patients were subjected to radical operation at the time of resection of the fistula, and 1 of these failed to survive.

#### DUODENUM

Perforated duodenal ulcer is again discussed by Graham and Tovee.<sup>28</sup> Of 114 patients admitted in a fifteen-year period to a service of the Toronto General Hospital, 111 were operated on, with 7 fatalities, a mortality of 6 per cent. Three patients not operated on, for reasons that seemed justifiable, died. The ratio of males to females was 107/7. All the patients came from within a twenty-five-mile radius, and all had had recent perforations. The danger of long-distance transportation in such an emergency is stressed. Graham and Tovee urge proper preoperative preparation in patients who arrive in poor condition. All the perforations were closed with omental tabs held in place by three catgut sutures, on the theory that fibrinous sealing is the aim of operation. The age of the patients varied from sixteen to eighty-three years and averaged forty-seven years. These authors are inclined to believe that age is not too important as a factor in mortality. In 34 of 59 cases in which cultures were taken from the peritoneal cavity, no organisms were grown. Drainage of the abdominal cavity was used in only 14 cases. Spinal and Pentothal Sodium anesthesia is preferred. These authors are adamant in insisting on the danger of a more radical procedure than simple closure of the perforation.

Price and Lee<sup>29</sup> closed experimental perforations in dogs' stomachs with omental tabs. All the closures made by omentum with an intact blood supply were successful. In many of the cases in which the tamponade was made with free omental grafts, the grafts became necrotic and leakage occurred.

Gray and Sharpe<sup>30</sup> followed the course of 52 of 62 patients who had been operated on for massive hemorrhage from duodenal ulcer by the Devine exclusion procedure. Five per cent of the patients failed to survive the operation. Forty per cent of

the survivors had later symptoms. The older patients did better than the younger ones, 18 of 21 fifty years of age or under having later symptoms, whereas only 3 of 16 over fifty did so. These authors conclude that this procedure may be justifiable in the older age group. They admit that it is a poor operation for duodenal ulcer, since only 60 per cent of the 52 patients remained symptom-free during the period of observation.

Colp et al<sup>21</sup> report the comparative immediate results in two series of patients subjected to subtotal gastrectomy for duodenal ulcer. In 79 patients operated on between July 1, 1937, and June 30, 1940, there was an operative mortality of 10 per cent, whereas in 94 patients operated on during the following three-year period, the mortality was 4 per cent. The authors believe that better management of the duodenal stump with preliminary and complementary jejunostomy accounted for the improvement in results.

Rienhoff<sup>22</sup> reports his results in 260 patients operated on for duodenal ulcer and followed for two to ten years. Two hundred and four patients (78 per cent) were considered well. Of the latter, complications developed in 32 (15 per cent), 22 of whom were subjected to further surgery. Thirty patients (12 per cent) were considered improved, and 4 of these were reoperated on. Twenty-one patients (8 per cent) were classified as unimproved, and 3 of these were reoperated on. The percentage of patients who remained well was higher in those with lowered gastric acidity than in those whose acidity continued high. Twenty-three patients (9 per cent) of the entire series developed anastomotic or jejunal ulcers. Rienhoff states that half the distal stomach with the pylorus was removed in all the patients, a short-loop antecolic anastomosis being used. In over 75 per cent of the cases, the ulcer was not resected. The operative mortality in the first 100 cases was 5 per cent. There were no deaths in the last 160 patients operated on, but some of these operations were too recent for end-result studies.

Lahey<sup>23</sup> advises in some duodenal ulcer operations the use of a T tube in the common bile duct with a long arm through the papilla of Vater for ease of identification in difficult dissections. In his discussion of Rienhoff's paper, he brings out the likelihood of better results if the ulcer can be safely included in the resection. Marshall<sup>24</sup> believes that a more radical resection of the stomach than Rienhoff uses would result in fewer jejunal ulcers.

McKuttrick, Moore and Warren<sup>25</sup> analyzed the gastric resections for ulcer in the Massachusetts General Hospital from 1936 to 1943. There were 2 deaths in 106 cases of gastric ulcer and 10 deaths in 218 cases of duodenal ulcer — an over-all operative mortality of 3.7 per cent. These authors stress the dangers that arise in management of the duodenal stump in duodenal ulcer and recommend more frequent use of a two-stage procedure. The Finsterer

subtotal gastrectomy for exclusion is done as the first stage, and the removal of the antrum and the first portion of the duodenum as the second stage six weeks later. St John<sup>26</sup> in his discussion of this paper reports the results in the Presbyterian Hospital, New York City between 1939 and 1943. The gastric and duodenal ulcer operations are grouped together, with an over-all mortality rate of 3.7 per cent in 299 cases.

Lannin<sup>27</sup> gives an excellent review of the development of the modern concept of adequate resection of the stomach for duodenal ulcer. Experimental work based on duodenal ulcers in dogs produced by the method of Code and Varco<sup>28</sup> showed that the only procedures that always cured these ulcers were gastrectomy with sacrifice of the distal two thirds of the stomach and the Finsterer exclusion operation with removal of the antral mucosa. These writers further show by their experiments that the anastomosis must be placed as close as possible to the ligament of Treitz. They give evidence that antecolic anastomosis results in jejunal ulcer in direct proportion to the length of the afferent loop. This is supported by a series of three hundred subtotal gastrectomies in patients with duodenal ulcer. With these features in mind, no anastomotic or jejunal ulcer has so far developed. They believe that this is due to three reasons: the distal two thirds of the stomach is sacrificed, no antral mucosa is left behind, and the anastomosis is made as near the duodenojejunal junction as is technically possible.

Dragstedt and Schafer<sup>29</sup> give a further report on the treatment of peptic ulcer by transthoracic vagus interruption. Thirteen patients with duodenal ulcer, 1 with gastric ulcer and 1 with gastrojejunal ulcer were treated by this method. Three of the patients with duodenal ulcer were later subjected to gastroenterostomy for persistent duodenal obstruction. All these patients were immediately relieved of their ulcer symptoms, since hypersecretion of gastric juice was eliminated, but 1 patient had a recurrence of symptoms after three months of relief. The patient with gastrojejunal ulcer required a prolonged medical regimen after vagus interruption and was only partially relieved of his symptoms.

Moore, Chapman, Schulz and Jones,<sup>30</sup> have been studying this attack on the ulcer problem at the Massachusetts General Hospital. Their preliminary report substantiates Dragstedt's claims. These patients are immediately relieved of ulcer pain. The procedure is particularly adaptable to the recurrent-ulcer group and may well supplant subtotal gastrectomy in cases of uncomplicated but intractable ulcer. The wisdom of using this operation for cicatricial stenosis of the duodenum is doubtful. It probably has a limited field in gastric ulcer owing to the high incidence of early cancer in these patients.

## SMALL INTESTINE

Cleland<sup>41</sup> measured the length of the small intestine in 100 cases at autopsy. It was impossible to determine that age, sex or disease had any bearing on the variations, which ranged from 4 to 11 meters. The physiologic processes of the subjects examined seemed undisturbed.

These data are particularly important to the clinician. Reports are often made on the successful removal of considerable lengths of the small bowel with apparent subsequent good health. On the other hand, patients may suffer a serious handicap from the loss of a relatively small segment of bowel. Occasionally this produces problems concerning nutrition, but the disturbance oftenest seen is one of persistent diarrhea. It is quite possible that the original length of the intestine in a given patient needing elimination of a segment of bowel may influence the postoperative course. A rapid intestinal rate of a functional type also plays a role in this problem.

Smith<sup>42</sup> has analyzed the experience in the Presbyterian Hospital in 1000 cases of intubation with the Miller-Abbott tube, which was successfully used in 751 cases and failed in 219, with the records incomplete in 30. It was employed prophylactically in 151 lesions of the small bowel and postoperatively in 84, and prophylactically in 108 lesions of the large bowel and postoperatively in 15, 153 intubations were for diagnostic purposes. Two or three cubic centimeters of mercury in the balloon is advised to aid the passage of the tube through the pylorus. There were complications in 140 cases—trivial in 129 and serious in 11. The tube required replacement in 54 cases.

Deering,<sup>43</sup> in reporting on his experience with the double-lumen tube in 200 cases, points out that the effectiveness of Wangenstein suction on a single-lumen nasal tube must not be forgotten. He believes that the Miller-Abbott tube should be reserved for extensive distention of the small bowel, the simpler method being more adaptable to the prevention of postoperative ileus and the relief of high intestinal obstruction.

Garlock and Crohn<sup>44</sup> analyzed the results in 164 patients treated for regional ileitis and ileocolitis. In 65 patients, the ileum was transected proximally to the disease and the distal end was inverted and dropped free into the peritoneal cavity, this being followed by ileotransverse colostomy. There were no deaths following this procedure, and recurrence of symptoms required extirpation of the diseased segment in only 9 cases. One-stage resection was done in 55 patients, of whom 9 died and 9 had recurrences. Twenty-five patients had two-stage resections, with death in 3 cases and a recurrence in 8. In 19 cases of ileocolitis, there were 2 deaths and 3 cases with recurrence.

In 19 patients who were subjected to resection

for regional ileitis by Bockus,<sup>45</sup> 3 died and 9 developed recurrent disease.

Cave<sup>46</sup> had 3 deaths, all from perforation of the ileum, in a series of 23 patients with regional ileitis. One of these died preoperatively, 1 a year after operation and 1 two years after operation. Seven of 80 patients operated on for ulcerative colitis had involvement of the terminal ileum. Cave calls attention to a rare form of chronic inflammation that he has encountered once, with a successful outcome. In this type there is a fibrinous envelope surrounding the intestine, which causes obstruction by infolding of the mucous membrane from outside pressure. Relief was obtained by the removal of the encapsulating structure.

Two unusual double intussusceptions of the ileum have been reported.<sup>47, 48</sup> Both cases were in boys, aged four and five years. The first patient following treatment for round worms developed intussusception of the ileum with a second loop extending into the original one. The second case was initiated by a lipoma in the wall of the ileum. The first patient recovered after reduction of the intussuscepted segments, and the second after resection and anastomosis.

Dearing et al.<sup>49</sup> present an interesting case history of a seventy-five-year-old man who was admitted with intermittent intestinal obstruction and weight loss. Study revealed a calculus in the ileum, which was successfully removed at operation. It weighed 70 gm, measured 5.5 by 5.5 cm, and consisted chiefly of calcium carbonate and calcium phosphate.

Stone<sup>50</sup> presents the results of studies on patients with massive melena. Of 72 patients varying in age from eleven months to seventy-nine years, 21 had a cause for the bleeding proved by examination, operation or autopsy, in 20 cases, a possible but not a definite cause was revealed, in 31 patients, no cause for melena could be found. Stone points out that the latter group of cases should be treated conservatively and future studies done. Exploratory laparotomy, he states, may be justified in a search for the cause in certain patients at a time of election.

In a study of cancer in the small intestine, Shallow, Eger and Carty<sup>51</sup> brought out the fact that in routine autopsies such lesions are found in the colon thirty-six times as often as in the small bowel. To 269 cases found in the literature they added 38 cases from the records of the Jefferson Hospital, Philadelphia. Carcinoma was most frequent in the duodenum and sarcoma most frequent in the ileum. The operative mortality, which was 44 per cent, was highest in the lesions of the duodenum and lowest in those of the jejunum.

To the above cases may be added 21 cases of malignant tumors of the small intestine studied by Fraser<sup>52</sup> in Glasgow. In his report, lesions of the duodenum were excluded and the ratio of carcinoma to sarcoma was 12/9.

Hanno and Mensh<sup>53</sup> report a case of intermittent massive melena of fourteen years' duration. The patient had been subjected to gastroenterostomy on an erroneous diagnosis. Bouts of hemorrhage continued and finally ended in death from acute anemia. Autopsy revealed as the cause of bleeding a leiomyoma of the jejunum 20 cm distal to the gastroenterostomy stoma.

Sibley<sup>54</sup> reviews the literature on Meckel's diverticulum and reports 10 cases from his own experience. Emphasis is placed on the high incidence of gastric mucosa found in these lesions and on the frequency of dyspepsia resulting from hypersecretion at this level in the gastrointestinal tract. He emphasizes that the possibility of this condition as a cause of abdominal pain is frequently overlooked. Gendel and Beaver<sup>55</sup> have successfully treated a patient with Meckel's diverticulum still attached to the umbilicus. This case was complicated by gastric mucosa and by a wood splinter in the diverticulum that caused intestinal obstruction. An incidental finding of early acute appendicitis seemed to play no recognizable role in the symptomatology. An additional case of Meckel's diverticulum containing calculi has been reported by Allen and Donaldson,<sup>56</sup> making a total of 11 recorded cases.

#### COLON

DeBakey and Carter<sup>57</sup> discuss penetrating wounds of the abdomen and bring out the fact that the mortality rate in World War I was 45 per cent, as compared with 15 to 20 per cent in World War II. They attribute these better results to three chief factors: ample supplies of whole blood and plasma, a larger number of well trained surgeons in the forward area, and the widespread use of exteriorization of colon wounds, routine proximal colostomy and proper drainage of the pelvis in wounds of the rectum. The authors lay too little emphasis on the effects of better selection and distribution of personnel by the Office of the Surgeon General.

Poth<sup>58</sup> has made an exhaustive report on collected data relating to the use of sulfasuxidine and sulfathalidine in surgery of the colon. The effect of these drugs in preoperative cleansing of the bowel has, in the opinion of many surgeons, proved to be a good adjunct to careful colonic surgery.

Newton and Blodgett<sup>59</sup> compare the results in two series of colon operations done at the Peter Bent Brigham Hospital. In 78 resections without the use of sulfasuxidine, there were complications in 45 and 15 deaths. In 36 patients treated preoperatively with sulfasuxidine, there were complications in 9 cases and 1 death following operation.

Bargen<sup>60</sup> has used both sulfasuxidine and sulfathalidine extensively in intestinal disease. He points out the advantage of the lower toxicity of sulfathalidine and reports that some patients sensi-

tive to sulfasuxidine tolerate sulfathalidine well. He believes, as we do, that sulfathalidine is the superior drug. It gives a better preparation of the bowel and is less apt to cause bleeding from the growth and nausea to the patient.

Coller and Vaughan<sup>61</sup> report a series of 173 consecutive cases of carcinoma of the colon recently treated at the University of Michigan Hospital. Twenty-eight cases (16 per cent) were not resectable. Of the 145 cases considered operable, 28 (19 per cent) had gross metastases to the liver or peritoneum. There were 112 patients whose spread of disease appeared to be limited to the resectable nodal regions. In this group there was only 1 death, which followed an attempt to remove widespread disease. These authors preferred the two-stage attack on the right colon if the lesion was large or infected or produced obstruction and if the patient was debilitated. One-stage procedures were done on more favorable lesions of the right colon and in all other segments. Fourteen patients had the Rankin obstructive modification of the Mikulicz operation. All the others had primary anastomosis, which in 68 cases was of the aseptic and in 52 was of the open type. Delayed wound closure was employed when there was gross contamination or after the open method of anastomosis. Sulfonamides were not used in the peritoneal cavity. Transverse incisions with fine-wire closure and early ambulation are believed to have contributed to the good results.

White and Amendola<sup>62</sup> report the results of colon resection for malignant disease in the Roosevelt Hospital, New York City. It appears that primary aseptic suture and proximal decompression resulted in half the deaths that occurred in modifications of the Mikulicz type of resection. These writers stress the shorter period of morbidity and the greater comfort to the patient in the primary anastomosis group.

Berson and Berger<sup>63</sup> found the incidence of multiple carcinomas of the colon to be 5 per cent of all their colonic lesions. Thirteen patients had two areas of carcinoma at the same time, and 3 had three areas. Polyps were present in 25 per cent of the patients having one area of carcinoma and in 38 per cent of those with multiple lesions. Sixty-seven per cent of the polyps in the multiple group had undergone malignant degeneration. These authors point out the need for thorough investigation of the entire colon and the importance of follow-up studies.

Pregnancy complicating carcinoma of the colon is discussed by Banner, Hunt and Dixon.<sup>64</sup> They found 62 cases in the literature and added 7 from the Mayo Clinic. They point out that the usual symptoms of carcinoma of the colon, such as nausea and constipation, are often associated with pregnancy and are therefore overlooked. They are impressed with the ease of delivery after abdominoperineal resection and the apparent safety of



cesarean section in the presence of a colostomy

Finn and Lord<sup>65</sup> report a case of carcinoma of the sigmoid with obstruction occurring in a thirty-one-year-old tripara who was in the sixth month of pregnancy. The lesion was treated by a three-stage procedure and the patient was successfully delivered at term.

Wangensteen<sup>66</sup> has anastomosed the colon to the rectal ampulla after resection in 24 patients for carcinoma of the rectum and rectosigmoid and in 3 patients for ulcerative colitis. There were 2 hospital deaths in the cancer group. He drains the pelvis posteriorly and expects a temporary fistula. The sphincter control was good in all cases. Three of the patients with cancer had local metastases to the liver, which were excised. Five of the 22 survivors had developed local pelvic recurrences at the time of the report. Wangenstein admits that fixed tumors require abdominoperineal resection.

Bacon<sup>67</sup> states that in 208 cases in which resection of the rectum was done for carcinoma he preserved the anal sphincter in 80 per cent. He has modified the combined abdominoperineal operation of Babcock to include preservation of the sphincter, and believes that this operation does not influence local recurrence provided that the muscles are not involved. He agrees with Babcock that perineal colostomy is superior to the abdominal type. His resectability rate was 81 per cent, and the mortality 5.5 per cent.

The increasing tendency to preserve the anal sphincter in carcinoma of the rectosigmoid and high rectum should be based on sound cancer surgery. One may make a low anastomosis and do Bacon's operation, or even extirpate the rectum through the perineal route with revision of the sphincter, under two conditions—in patients with early low-grade localized lesions at a suitable level and in those with an incurable spread of disease. Local recurrence is justifiable only in the latter group. The use of drainage to the pelvis incites a fistula, increases infection and produces subsequent stenosis of the suture line. If an adequate preparation is done before operation and the peritoneal reconstruction is made with room for adequate seepage of serum into the peritoneal cavity, the results without drainage are better.

Griffin, Barton and Meyer<sup>68</sup> found that volvulus of the sigmoid accounted for 8 per cent of the obstructions of the large bowel in a series of 458 cases admitted to the Cook County Hospital. Twenty-five records were analyzed in detail. There seemed to be two distinct types of sigmoid volvulus. There were 7 acute cases, mainly in young patients with an average of twenty-four hours of symptoms and no previous history of bowel disturbance. Eighteen cases were classified as subacute and were in the older age group. These patients were ill for an average of one hundred and two hours before admission, and many of them had had pre-

vious attacks. These authors call attention to a characteristic so-called "ace of spades" appearance in the roentgen-ray film after barium enema. The mortality in this series was 40 per cent. The authors stress early diagnosis and early resection and advise against conservative measures.

#### PANCREAS

Morton<sup>69</sup> has given an excellent discussion on acute pancreatitis. Two thirds of the cases are those of acute pancreatic edema, and 60 per cent of these are associated with lesions in the biliary tract. The serum amylase is always elevated early in this type of the disease. Conservative treatment is indicated, and the mortality is low. Recurrent attacks are frequent. After recovery from the acute phase the biliary system should be studied, and if gallstones are present, they should be removed. Pancreatic necrosis accounts for the other third of patients with acute pancreatic disturbance. In this type of case the serum amylase may not be elevated and the symptoms are severer. Morton believes that surgery should be undertaken to establish adequate drainage of the pancreatic area as early in the disease as is compatible with the patient's condition. All nine patients with this necrotizing type of pancreatitis who were treated conservatively died, whereas of those operated on for drainage 45 per cent recovered. Diabetes followed in a certain number of the recoveries. This author calls attention to the precipitation of acute pancreatic edema by operation for duodenal ulcer penetrating into the pancreas.

Shallow et al.<sup>70</sup> report a successful outcome in an extremely ill woman of fifty-five who had pancreatic necrosis of eight days' duration. In addition to a large pancreatic abscess, there were two abscess cavities in the quadrate lobe of the liver. They believe that penicillin and sulfadiazine aided in the recovery on the basis of the types of organisms cultured.

Ten patients with pancreatic collections operated on with recovery are reported by Pinkham.<sup>71</sup> He discusses the differential diagnosis between so-called "true cysts," on the basis of proliferative changes due to neoplasm, hydatid disease, congenital defects and retention due to obstruction of pancreatic ducts, and "pseudocysts." The latter type should be referred to simply as collections secondary to pancreatic trauma, inflammation or necrosis.

Whipple<sup>72</sup> records his results in pancreaticoduodenectomy. He believes that the one-stage procedure has many advantages over his original two-stage operation. Twenty-two patients with cancer and 5 with calcification of the pancreas were subjected to radical operation. In 8 cases in which the two-stage operation was done there were 3 deaths, whereas in 19 one-stage procedures there were 6 deaths. A patient who had islet-cell carcinoma was apparently well five years after opera-

tion Whipple<sup>7</sup> advises implanting the common duct in the jejunum, with implantation of the pancreatic duct slightly lower down. This avoids the possibility of bile leakage and eliminates the debated question concerning the importance of re-establishing pancreatic continuity with the gastrointestinal tract.

Orr and Walker<sup>73</sup> stress the relative infrequency of carcinoma of the duodenum and report a case of a successful Whipple procedure in one stage. They point out that most of the carcinomas in this region start in the ampulla of Vater and are improperly recorded as duodenal lesions.

Strode<sup>74</sup> reports a successful Whipple operation for carcinoma that was primary in a duodenal diverticulum.

Brunschwig et al<sup>75</sup> record a case of total pancreatectomy, total gastrectomy, total duodenectomy, splenectomy, left adrenalectomy and omentectomy in a diabetic patient fifty-three years of age. The patient required no increase in the amount of insulin used preoperatively. He died of widespread carcinomatosis three and a half months after operation.

266 Beacon Street

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 32121

#### PRESENTATION OF CASE

A twenty-three-year-old woman was admitted to the hospital complaining of vaginal bleeding.

She was in the fourth month of pregnancy. Ten days before admission the fetus was said to have died, and six days later vaginal bleeding began and increased up to admission.

The past history revealed that the patient had been in good health until a year before admission. At that time she had a spontaneous abortion at about the third month of pregnancy. She had received a plasma transfusion.

On physical examination the patient was well developed and well nourished and in no acute discomfort. The heart and lungs were normal. The uterus showed enlargement consistent with a four months' pregnancy. There was a foul, blood-stained vaginal discharge.

The temperature was 101°F, the pulse 80, and the respirations 20. The blood pressure was 110 systolic, 50 diastolic.

The red-cell count was 4,240,000, with 12.2 gm of hemoglobin. The white-cell count was 21,400, with 86 per cent neutrophils, on smear, many band forms were seen and the platelets were decreased. On the first hospital day the sediment from a catheterized specimen of urine contained 25 red cells, an occasional white cell and 5 epithelial cells per high-power field.

Soon after admission the patient was sedated with codeine and aspirin and given 6 gm of sulfadiazine. Penicillin was ordered, 16,000 units every two hours. Later the dose was increased to 64,000 units every two hours. During the afternoon of the first hospital day the temperature rose to 105°F. She had a chill and a few hours later spontaneously passed a macerated fetus. Fifteen minutes afterward an ampule of Pituitrin was administered intravenously, and a half ampule at fifteen-minute intervals for two more doses. The placenta, which was yellow, friable and necrotic, was passed at the time of the second dose. Eleven milligrams of morphine were given. After the abortion the patient complained of severe chest pain. The blood pressure fell steadily

to a level of 40 systolic, 0 diastolic. An intravenous injection of dextrose in saline solution was begun, and 1 unit of plasma was given. The patient's condition improved somewhat, and the intravenous drip was continued. Four hours later she was found in shock, being only slightly responsive, with a blood pressure of 40 systolic, 0 diastolic, and a pulse of 120 to 150. Another unit of plasma was given, followed by a transfusion of whole blood. A few hours later another whole-blood transfusion was given.

During the second hospital day, the patient became more responsive. She complained of nausea and severe generalized aching. Despite continuous intravenous drip and hypodermoclysis, she remained dehydrated. The blood pressure rose to about 50 systolic, with a pulse of 145 that was of better quality. She remained oliguric, only 30 cc of urine being obtained by catheter during twenty-four hours. The urine was cloudy, light amber and acid and gave a + test for albumin. The quantity was insufficient for measurement of the specific gravity. There was no sugar or diacetic acid. The sediment contained a rare coarsely granular cast, a rare red cell, an occasional white cell, 5 round cells and 10 epithelial cells per high-power field. No crystals were seen. The urine was sterile. A marked generalized flush appeared, with definite circumoral pallor. She vomited about 150 cc of grayish material mixed with mucus. She manifested air hunger, the respirations being deep and sighing. She was not cyanotic. The lungs were clear. She was given a transfusion of Rh— blood, 3500 cc of fluid, 7 gm of sodium bicarbonate and 100 cc of cortical extract.

On the third hospital day, periorbital edema appeared but the lungs remained clear. The blood pressure rose to 80 systolic, 50 diastolic. The generalized erythema became more punctate. Mild air hunger persisted. There was marked epigastric tympany, with fullness. Peristalsis was sluggish but of normal pitch. A few drops of urine were obtained by catheter. The sediment contained many white cells and a few red cells per high-power field, there were no casts or crystals. The patient was alert. Herpes labialis appeared. Cystoscopy revealed a normal bladder containing no urine. Both ureters were easily catheterized but no urine was obtained. The ureteral catheters were left in place.

On the fourth hospital day the serum protein was 3.5 gm per 100 cc. A Schultz-Charlton test was negative. The patient became semicomatose, with fibrillary twitching of the entire body. A subconjunctival hemorrhage appeared in the right eye. Early on the fifth hospital day she had a severe generalized convulsion and expired.

#### DIFFERENTIAL DIAGNOSIS

DR. ARTHUR T. HERTIG: \* This case may be summarized as one of a young woman who had had no

\*Pathologist Boston Lying in Hospital and Free Hospital for Women Brookline

previous full-term pregnancies but had had one previous miscarriage of spontaneous origin and who came in with a septic inevitable abortion in the fourth month of pregnancy. The first thing of interest is the fact that this spontaneous inevitable abortion was septic. That in itself is an extremely unusual fact. Very seldom do spontaneous abortions show a septic course. I assume that this was a spontaneous rather than an induced abortion and that she was febrile from it rather than from some other inflammatory process.

Another interesting factor is that the patient bled so soon after the fetus died. The latter event occurred about ten days before delivery, and she began to bleed six days later, four days prior to admission. Usually it takes longer after fetal death for the sequence of events resulting in abortion to take place. The most immediately interesting thing about this patient is that she delivered spontaneously and then required two ampules (2 cc) of intramuscular Pituitrin in divided doses to effect delivery of the placenta. Pituitrin was indicated since it is good obstetric procedure not to invade the uterus in a case of septic abortion because of the chance of spreading the infection.

The first thing of importance with respect to her death seems to me to be the fact that she reacted badly, almost immediately, to the administration of Pituitrin. It must be remembered too that there could have been other causes for the patient's going into shock, one being unrecognizable or undiagnosed rupture of a viscus, specifically a ruptured uterus. I take it that the clinicians involved were satisfied that the patient had no ruptured internal viscus. She certainly had no external bleeding or peritoneal signs to go with a ruptured uterus. Hence, I should say that in all probability she did not have a ruptured uterus, although that must be considered. My impression at this point is that the patient had profound Pituitrin shock and was one of the very rare persons sensitive to even moderate doses of this drug.

The next fact of importance is that prior to delivery a catheter specimen of urine contained 25 red cells per high-power field. Whether the red cells came as a result of the trauma of catheterization or whether she actually had a hematuria, I do not know. That is an important point to consider in view of the oliguria and anuria that developed later. A significant fact clinically is that she was in general shock from which she did not respond well despite intravenous fluid, plasma transfusion and two whole-blood transfusions. It is of interest to ask why she did not respond to an apparently adequate amount of fluid and blood in the absence of a ruptured viscus and in the absence of any profound loss of blood. These features help to make the diagnosis of Pituitrin shock.

The next point to inquire about is whether this patient was Rh—, and I assume that she was since

they gave Rh— blood on the third transfusion. If she was Rh—, the next thing to determine is whether she had been previously sensitized by the Rh factor either from a previous transfusion or by the previous pregnancy, which aborted at three or four months. So far as I know there are no examples of isoimmunization in an Rh— patient by a pregnancy that did not persist over three or four months. She may, however, have been given Rh+ blood on the two transfusions before the Rh— transfusion. Is there any information about that?

DR WADE VOLWILER They were Rh+.

DR HERTIG Then that is a possible factor in her death, namely, that she had been sensitized to Rh+ blood, developed agglutinins and reacted fatally on perhaps the second of the two transfusions. Were both of them Rh+?

DR VOLWILER Yes.

DR TRACY B MALLORY How long was the time interval between the first and the last transfusion?

DR VOLWILER Not more than three days.

DR HERTIG And the time interval between the first two was a matter of hours?

DR VOLWILER Yes.

DR HERTIG So on the basis of the history one can rule out reaction of the patient to Rh+ blood after sensitization. There had not been time for her to have become sensitized. Furthermore, she does not appear to have had an ordinary transfusion reaction.

The next point of clinical significance is the fact that she had oliguria, which progressed to almost complete anuria. In a pregnant patient who had previously been transfused that could suggest two things—transfusion reaction, which can largely be ruled out, and bilateral symmetrical cortical necrosis of the kidney. Renal cortical necrosis was probably brought on by severe prolonged ischemia, induced by Pituitrin sensitivity and resulting in contraction of the precapillary arterioles throughout the body, particularly the afferent and efferent arterioles of the kidney. Hence my diagnosis is bilateral symmetrical cortical necrosis of the kidney. The clinical course is typical. She died at about the average time, namely five days. I do not believe that she had a transfusion reaction, nor do I believe that she had a ruptured internal viscus. The profound, prolonged shock is difficult to evaluate.

DR MALLORY Are there any questions or other diagnoses that anyone would like to suggest?

A PHYSICIAN Could syphilis be connected with this story in any way?

DR MALLORY I believe not. The Hinton test was negative.

DR W SCHIER WILSON Were hematein crystals seen in the urine on any occasion?

DR MALLORY There is no record of them.

DR HERTIG In fact, it states that there were no crystals of any sort. I should have said that this case might possibly be one of sensitization or sen-

sitivity to a sulfonamide because of the fact that some persons are sensitive to such drugs and react to relatively small doses. The patient received 6 gm of sulfadiazine. Such patients, — that is, the few whom I have seen, — die on the average in five or

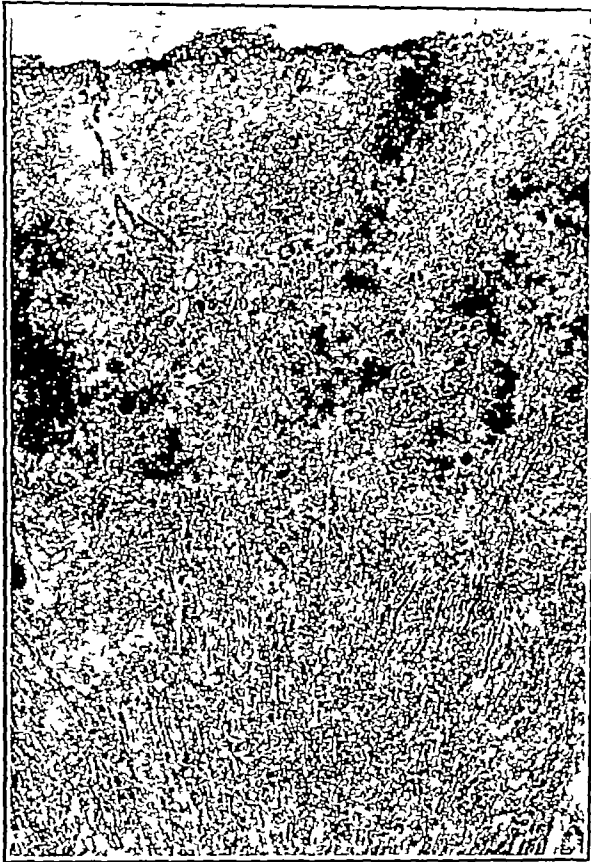


FIGURE 1

six days with anuria. In my opinion, however, there should have been some evidence of sulfonamide crystals in the urine were this case one of sensitivity to one of these drugs.

#### CLINICAL DIAGNOSES

Spontaneous abortion with septicemia  
Uremia

#### DR. HERTIG'S DIAGNOSIS

Bilateral cortical necrosis of kidneys

#### ANATOMICAL DIAGNOSES

**Symmetrical necrosis of renal cortex.**  
Infarction of adrenal gland, bilateral  
Subinvolution of uterus  
(Uremia)

#### PATHOLOGICAL DISCUSSION

DR. MALLORY Except for the difference of sex and the presence of pregnancy this case is quite

reminiscent of scores of cases that many of us saw overseas during the last couple of years and in which the pathologic lesion is entirely different from that Dr. Hertig has suggested. Almost any patient with severe traumatic shock who has received multiple transfusions runs a considerable risk of dying with delayed anuria and a clinical picture that, so far as I can see, is indistinguishable from the late stages of this story.

The kidneys of this patient were slightly enlarged. The external surfaces were vaguely mottled, poorly defined purplish areas being separated by irregular yellow areas. The appearance of the cut surface was much more striking. The entire cortex was discolored. The major part of it was bright red, but there were scattered, irregular, yellow areas in the midst of the hemorrhage. Under low power, the cortex showed dark areas representing hemorrhage (Fig. 1). These stopped abruptly at the junc-



FIGURE 2

tion between the cortex and pyramid. With higher power, the striking feature comprised the blood vessels. In a typical glomerulus and its afferent arteriole (Fig. 2), the wall of the arteriole appeared black, it was completely necrotic, part of it solidly thrombosed and part having a lumen. The fibrin of the thrombus extended over into several of the loops of the glomerulus. The tubules were widely separated by hemorrhagic stroma. The adrenal glands weighed 40 gm and were completely necrotic, with hemorrhagic borders (Fig. 3). The picture essentially is like that of the Waterhouse-Friderichsen syndrome. The arterioles in the capsules of the

adrenal glands were necrotic (Fig. 4). The change is identical with that present in the kidneys.

Dr. Hertig's diagnosis of symmetrical cortical necrosis is substantiated, and as he pointed out, that is the usual lesion that one would expect in a patient who developed delayed uremia immediately after delivery. The lesion that we saw with shock in Europe was entirely different. There was no

the initial lesion was in the precapillary arterioles of the kidney. The precapillary arterioles elsewhere in the body, whether in the bowel, adrenal gland or pituitary gland or elsewhere, also showed involvement. The massive cortical necrosis was apparently due to retrograde or diffuse thrombosis of the small erect arteries, but the initial lesion began in the small precapillary arterioles. Is that your impression?

DR. MALLORY: I do not feel competent to express an opinion. This is a fairly rare condition. At the time Dr. Hertig\* reported his cases four years ago he was able to collect about 70 cases from the literature. It is unquestionably not so rare as that suggests, because all of us know of unreported cases.

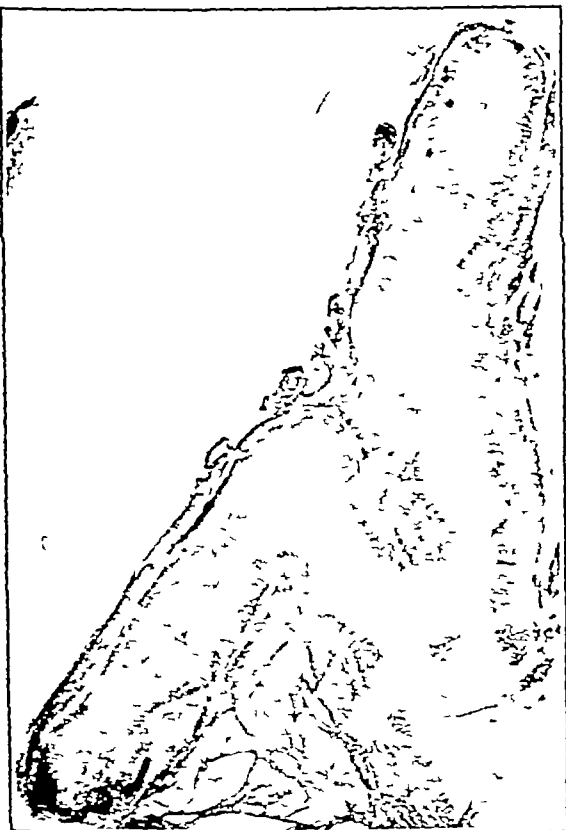


FIGURE 3

necrosis of the cortex. The degenerative changes were found in the lower part of the nephron, the ascending loop of Henle in particular, and the tubules were filled with hemoglobin casts just as they are in a transfusion reaction.

Have you any further comment, Dr. Hertig?

DR. HERTIG: I have seen two cases like this. One patient died on the fifth day, and the other on the eleventh day post partum. The former case was exactly like the one presented here. The patient who lived eleven days did so only by the heroic efforts of the house staff, who did several exsanguination transfusions. The entire renal cortex of the latter case was necrotic, but instead of being mottled red and yellow, it had a brilliant orange-yellow border around the periphery of the kidney, with only minute areas of viable tissue left. It is our impression from studying these cases that

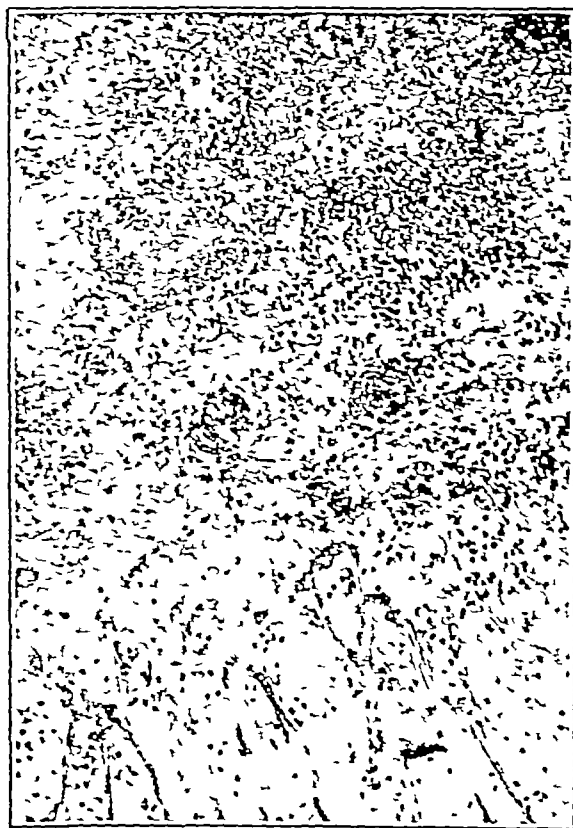


FIGURE 4

It was first described in relation to pregnancy, and it is still seen much more frequently in relation to pregnancy than in any other condition. It can occur in the male sex, and a condition that simulates it closely can be produced in animals by injecting a toxin derived from staphylococci, which have nothing to do with the genesis of the human lesion.

DR. DONALD S. KING: How much of a factor was the Pituitrin?

\*Sheldon, W. H. and Hertig, A. T. Bilateral cortical necrosis of kidney. *Arch. Path.* 34: 866-874, 1942.

DR MALLORY I do not feel capable of answering that Dr Hertig has said all that can be said

DR JAMES B TOWNSEND Have all the patients received Pituitrin?

DR HERTIG I do not know whether they have or not. Most cases, however, follow so-called "toxic separation" of the placenta. In this case the clinical picture was so striking immediately following administration of Pituitrin that the drug seems to have had something to do with it. We know of course that this drug does contain a pressor substance affecting blood vessels and hence could have been the stimulus which caused the generalized arteriolar spasm that resulted, among other things, in cortical necrosis.

DR TOWNSEND Was any organism obtained from the blood ante or post mortem?

DR MALLORY No

DR HERTIG It must be pointed out that most cases of this condition in pregnancy are associated with toxic separation of the placenta, the underlying pathology of which is an acute atheromatous degeneration of the small arterioles of the placental site. This causes decidual necrosis and separation of the placenta from hemorrhage.

DR BENJAMIN CASTLEMAN Was either of your cases as early in pregnancy as this?

DR HERTIG No, they were in the seventh and eighth months.

DR MALLORY Occasionally, as Dr Hertig has pointed out, vascular lesions are found in other spots of the body besides the kidney. We were able to obtain the pituitary gland and cut a number of sections of it, but we did not find any vascular lesions.

## CASE 32122

### PRESENTATION OF CASE

A twenty-nine-year-old unmarried woman, a stenographer, was admitted to the hospital complaining of dizziness, nausea and vomiting. There is doubt concerning the validity of the history, since it was obtained from the patient, who was extremely ill.

She was well until about five weeks previous to admission, when she began to have intermittent attacks of weakness and dizziness. These apparently did not increase in severity or frequency. Five days previous to admission, while sleeping, she was suddenly awakened by severe vertigo, followed by severe nausea and vomiting. Immediately after this episode she felt weak. She again returned to sleep, but a few hours later she was awakened by the same symptoms, which lasted for about an hour. The following morning she had another similar attack. A local doctor was called, who thought that it was a gastrointestinal upset but later consulted a neurologist, who advised hospitalization. The pa-

tient stated that about twenty-four hours after the onset of her illness she developed a blurring of vision when looking through both eyes but not when looking through one. During the twenty-four hours previous to admission the doctor had started slow digitalization by mouth, giving 0.1 gm every four hours. An undetermined amount of this was vomited. The patient gave no history of rheumatic fever, previous recent infection or the taking of drugs or medicine.

Physical examination revealed a pale woman in considerable distress who was retching and restless. The pupils were normal. The fundi showed questionable binasal blurring. There was no hemianopsia. The extraocular muscles were normal. The neck was questionably stiff. The neck veins were not engorged. The left border of the heart was percussed at the anterior axillary line. The sounds were distant. No thrills or murmurs were detected. The cardiac rhythm was irregular. The apical rate was 108, the peripheral 65. The diaphragm was higher than usual. A few moist rales were heard over both lung bases. The liver edge was palpated 3 cm below the right costal margin and was tender, otherwise the abdomen was negative. There was no ankle edema, and the dorsal-pedis pulsations were normal. Vaginal examination revealed tenderness of both lateral fornices, there were no masses or discharge. The reflexes were sluggish, and Babinski's sign was absent. There was no sensory impairment.

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DR MALLORY I do not feel capable of answering that Dr Hertig has said all that can be said

DR JAMES B TOWNSEND Have all the patients received Pituitrin?

DR HERTIG I do not know whether they have or not. Most cases, however, follow so-called "toxic separation" of the placenta. In this case the clinical picture was so striking immediately following administration of Pituitrin that the drug seems to have had something to do with it. We know of course that this drug does contain a pressor substance affecting blood vessels and hence could have been the stimulus which caused the generalized arteriolar spasm that resulted, among other things, in cortical necrosis.

DR TOWNSEND Was any organism obtained from the blood ante or post mortem?

DR MALLORY No

DR HERTIG It must be pointed out that most cases of this condition in pregnancy are associated with toxic separation of the placenta, the underlying pathology of which is an acute atheromatous degeneration of the small arterioles of the placental site. This causes decidual necrosis and separation of the placenta from hemorrhage.

DR BENJAMIN CASTLEMAN Was either of your cases as early in pregnancy as this?

DR HERTIG No, they were in the seventh and eighth months.

DR MALLORY Occasionally, as Dr Hertig has pointed out, vascular lesions are found in other spots of the body besides the kidney. We were able to obtain the pituitary gland and cut a number of sections of it, but we did not find any vascular lesions.

## CASE 32122

### PRESENTATION OF CASE

A twenty-nine-year-old unmarried woman, a stenographer, was admitted to the hospital complaining of dizziness, nausea and vomiting. There is doubt concerning the validity of the history, since it was obtained from the patient, who was extremely ill.

She was well until about five weeks previous to admission, when she began to have intermittent attacks of weakness and dizziness. These apparently did not increase in severity or frequency. Five days previous to admission, while sleeping, she was suddenly awakened by severe vertigo, followed by severe nausea and vomiting. Immediately after this episode she felt weak. She again returned to sleep, but a few hours later she was awakened by the same symptoms, which lasted for about an hour. The following morning she had another similar attack. A local doctor was called, who thought that it was a gastrointestinal upset but later consulted a neurologist, who advised hospitalization. The pa-

tient stated that about twenty-four hours after the onset of her illness she developed a blurring of vision when looking through both eyes but not when looking through one. During the twenty-four hours previous to admission the doctor had started slow digitalization by mouth, giving 0.1 gm every four hours. An undetermined amount of this was vomited. The patient gave no history of rheumatic fever, previous recent infection or the taking of drugs or medicine.

Physical examination revealed a pale woman in considerable distress who was retching and restless. The pupils were normal. The fundi showed questionable binasal blurring. There was no hemianopsia. The extraocular muscles were normal. The neck was questionably stiff. The neck veins were not engorged. The left border of the heart was percussed at the anterior axillary line. The sounds were distant. No thrills or murmurs were detected. The cardiac rhythm was irregular. The apical rate was 108, the peripheral 65. The diaphragm was higher than usual. A few moist rales were heard over both lung bases. The liver edge was palpated 3 cm below the right costal margin and was tender, otherwise the abdomen was negative. There was no ankle edema, and the dorsal-pedis pulsations were normal. Vaginal examination revealed tenderness of both lateral fornices, there were no masses or discharge. The reflexes were sluggish, and Babinski's sign was absent. There was no sensory impairment.

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may produce this type of rhythm. There is also the patient who has ventricular paroxysmal tachycardia in an apparently normal heart. At least those that die may show at autopsy a mild fibrosis of the myocardium. It has been described in cases of calcified pericardium.

Finally there are the diagnoses that one of my naval medical friends calls "those in the back of the book" which can be listed, but I find no leads for any of those diagnoses.

There is some evidence of infection, such as the fever, leukocytosis, tender fornices on vaginal examination, tender liver and high diaphragm. Isolated myocarditis, the Fiedler type, has been described following various infections, including gonorrheal infection. We have no evidence of that here, and no vaginal discharge. There may be some undiagnosable infection of the abdominal cavity, but I do not know where it is.

In conclusion I am going to say that all the ordinary probabilities seem to be absent in this particular case. The evidence is somewhat more in favor of infection of the myocardium of an unknown type. There may perhaps be a lesion of the septum. There should be an enlarged and dilated heart, perhaps more so on the right than on the left.

Was the head examined at autopsy?

DR MALLORY: No.

DR SPRAGUE: Small cerebral thrombi may have been present. The patient really died of shock.

I should be interested to know whether the clinicians did any better than I have in deciding on a diagnosis.

DR WADE VOLWILER: The clinicians did not do so well. The patient apparently had some cardiac disorder, but no murmurs were heard. She was sent into the hospital by her physician as a brain-tumor suspect because of the dizzy spells. On the way to the hospital he discovered the arrhythmia and started digitalis. The ventricular tachycardia appeared when we were giving large amounts of quinidine, and the question came up whether one should stop or give more quinidine. The opinion was that we should not give more since the arrhythmia was produced during quinidine administration.

DR SPRAGUE: The theory behind quinidine and digitalis poisoning, especially that due to quinidine, is that, in the presence of bundle-branch block, the conducting mechanism of the heart, which permits the ventricles to discharge synchronously and all over at once, is interfered with. This allows parts of the ventricle to recover from their refractory periods at different times, so that where an abnormal beat is propagated through the ventricle it may re-enter through an area in the muscle that has barely recovered, which in turn sets up a circus movement through the ventricle. It may be initiated by the use of digitalis or quinidine or the combination.

DR ROBERT S. PALMER: I should like to ask Dr Sprague if he thinks that a large heart like this and

tachycardia could occur in a twenty-nine-year-old woman in five weeks without some previous damage in the heart. Perhaps congenital sclerosis of the coronary vessels would produce it.

DR SPRAGUE: We have no evidence that anything was wrong with the heart previously. The enlargement may have been almost entirely due to dilatation.

#### CLINICAL DIAGNOSES

Cardiac arrhythmia

Auricular flutter changing to ventricular tachycardia

Cerebral embolus?

#### DR SPRAGUE'S DIAGNOSES

Acute myocarditis, with involvement of inter-ventricular septum, of unknown etiology  
(? Fiedler type)

(Auricular flutter)

(Ventricular tachycardia and flutter)

#### ANATOMICAL DIAGNOSES

Idiopathic acute myocarditis (? influenzal myocarditis).

Pulmonary emboli, multiple

Mural thrombi: right auricle and right ventricle

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The autopsy on this patient showed a heart that was not hypertrophied and that was only moderately dilated. The liver was normal in size. The spleen was almost completely atrophic, weighing only 20 gm. The liver on section showed prominent central markings of the so-called "nutmeg" type. On opening the pulmonary artery, emboli were found in considerable number, and on going back to the heart, we found mural thrombi in the right auricle and right ventricle. The myocardium showed discoloration in numerous areas, particularly, as was prophesied, in the interventricular septum. This showed patchy gray spots that felt rather firmer than normal. Since the coronary arteries were completely normal, we strongly suspected that myocarditis was present. This was later confirmed microscopically.

This is a section of the myocardium (Fig 1). There are large areas from which the muscle cells have disappeared almost completely and in which only a few swollen hyalinized portions of fibers persist. Over to the right the fibers are still present but are obviously abnormal. The striations have been lost, there is central vacuolization in some, and they stain more intensely than normal. A rather striking feature of the section, which does not show in the photomicrograph because of inadequate magnification, is that some of these persistent muscle fibers contain a great many nuclei, sometimes five or ten in a single cell, much like the multinucleated giant cells one sees in degenerating skeletal muscle.

Mitotic figures are never found in muscle fibers after infancy, but the nuclei multiply amitotically by budding and fission. This occasionally occurs in heart muscle, but by no means so frequently as in striated voluntary muscle.

So we have here a severe myocarditis unassociated with proved infection anywhere else in the body. The valves were entirely negative. There was nothing in any of the organs to suggest rheumatic fever.

never personally seen such a case out of several score of cases of sulfonamide myocarditis. In my experience they have uniformly shown an interstitial myocarditis with little or no degeneration of the muscle fibers. I consider that a highly improbable etiology here.

One other cause of myocarditis was brought to our attention here in Boston a couple of years ago by Finland, Parker, Barnes and Jolliffe,<sup>3</sup> who reported

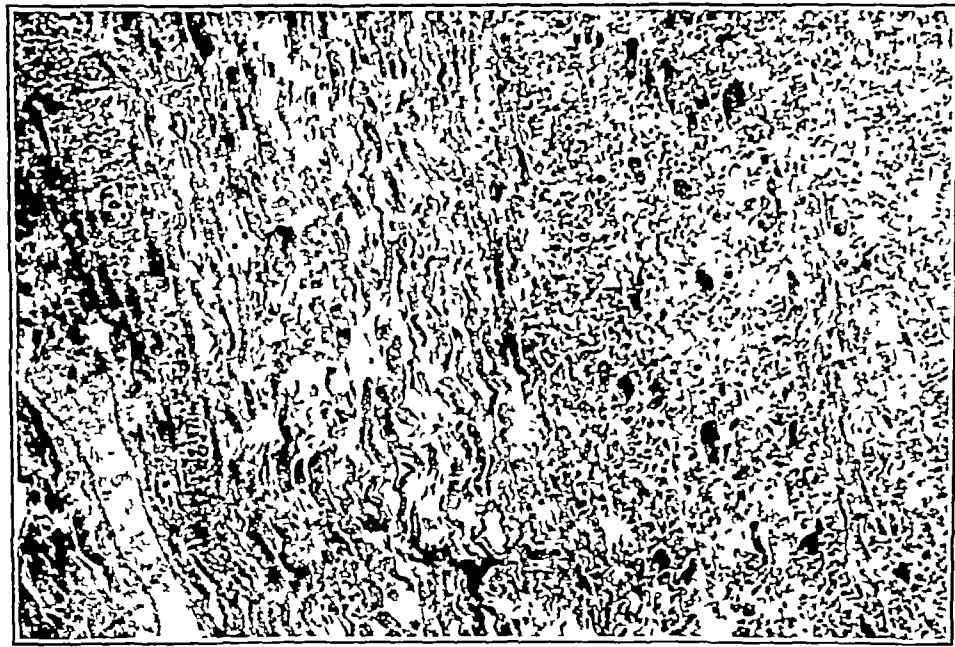


FIGURE 1

It could be described and catalogued as “isolated,” meaning merely that no other pathologic lesion was found in the body to account for it. An equally good term is “idiopathic,” because, after all, we know nothing whatever of the etiology in a great many of these cases. Myocarditis does appear in a rather wide variety of infections, such as meningococcal and streptococcal infections, but only irregularly and infrequently. The only common causes of myocarditis are diphtheria and rheumatic fever. It is rare that rheumatic fever produces massive necrosis of muscle such as you see here. Diphtheria commonly does, but there is nothing in the history to permit us to suppose that this girl had diphtheria.

A form of myocarditis due to sulfonamide therapy has become well known to pathologists in the last three or four years. It has not attracted a great deal of clinical attention so far as I am aware. Myocarditis with extensive necrosis of muscle fibers has been attributed to sulfonamide injury.<sup>2</sup> I have

two cases of myocarditis immediately following infection with influenza A virus. Inasmuch as at the present time there is a mild epidemic of influenza A, it is a possibility in this case, perhaps the best guess one can make, but we have no proof of it.

DR SPRAGUE: As far back as 1921 Fiedler's myocarditis was described following influenza, so that it seems quite likely.

DR GEORGE C. COTZIAS: If it were trichinosis, would one have any difficulty in finding the organism?

DR MALLORY: One should have no difficulty in demonstrating the parasites in a case of this severity.

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## NEW A.M.A. PROGRAM

THE new National Health Program of the American Medical Association and its scheme to establish minimum standards of acceptance for prepayment medical-care plans and to create a voluntary federation — Associated Medical Care Plans, Incorporated — are described in an editorial in the February 23 issue of the *Journal of the American Medical Association*, which should be thoughtfully read by all physicians

The National Health Program is a great improvement over the original fourteen-point program approved by the Board of Trustees last summer. Many of the obvious omissions in the latter, some of which were pointed out in an editorial appearing in the August 16 issue of the *Journal*, have been in-

cluded in the new program. Unfortunately, however, no reference is made to the need for improving the quality of medical care, in other words, it still seems to be taken for granted that all licensed physicians are equally well qualified to care for the sick.

Undoubtedly the standardization of medical-care plans will do much to ensure the success of such organizations, which in the past have enjoyed varying fortunes owing to a lack of sound actuarial data. Such figures are now becoming available, — for example, those concerning Massachusetts Medical Service, a pre-eminent successful venture, — and will be supplied by a new department of the American Medical Association — the Division of Prepayment Medical Care Plans — for the purpose of reorganizing nonacceptable plans or of creating new ones. One of the most significant steps is the formation of the voluntary federation, the chief aim being co-ordination of and reciprocity among all such medical-care plans. This should permit transference of subscribers from one plan to another and the rendering of service to subscribers outside their home states, all of which should encourage the acceptance of such plans by large national industrial organizations. Furthermore, a federation of this sort should be able to conduct a well co-ordinated and effective campaign of public education.

The American Medical Association appears to have initiated a constructive and promising program for improving the health of the Nation and for providing means of meeting the costs of medical care. It is to be hoped that this program will answer much of the criticism that has been directed at so-called "organized medicine" during the last few years.

## "TO DO SOMETHING FOR THE WELFARE OF MANKIND"

THE twenty-seventh annual report of the Commonwealth Fund accounts for the spending of \$1,418,056. This sum is divided between the Fund's special programs and a group of more diverse and various grants. The largest amounts in the first category were appropriated in the interest of public health and the further extension of the now well known rural-hospital program. Another hospital

is to be constructed, in Sikeston, Missouri, and a new experiment in regional medical organization is planned for the area surrounding Rochester, New York. Smaller, but still significant amounts were devoted to mental health, education and publications. The special grants for medical research, war relief and miscellaneous purposes total \$677,457. By far the greater amount of the latter expenditures continued

to be for medical interests and activities. These are the items that appear at the end of the report, where they are often read first by those interested in where and how money is being awarded. It is probably intended, however, that a reading of the foreword precede indulgence in the gross figures of distribution.

As in previous reports, the foreword suggests why money is being spent where it is. It is a thumbnail essay on the difficulties and uncertainties that currently face medical practice and education. It contains several incisive observations, such as, "No short-cut to the integration of specialized knowledge into comprehensive medical care has yet been devised." and "the practical details for a coherent plan for the encouragement and support of research remain to be worked out." It is then recognized that these are serious questions and that they are not likely to be solved in financial terms alone. Although the foreword emphasizes that what the Fund can do is a small part of what must be done, it states the minimum objectives of the Fund as follows: sound training for professional and technical workers in strategic phases of health maintenance, the broadening and integration of the basic concepts of medical care so that it may become truly comprehensive, and the practical encouragement of human curiosity as the fountain-head from which medical knowledge renews itself.

The health of the Nation is a vast borderland between a philosophy and a discipline, between sociology and medicine. In it there are many mansions, some old ones with outworn and useless concepts, some new ones, unfinished and with untried architecture. There are other comfortable and livable houses in which the tenants have kept in touch with the practical realities of the world

and are contributing to the evolution of the human race. The Commonwealth Fund continues to house such tenants.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

George L. Schadt, *Chairman*  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

### MASSACHUSETTS MEDICAL SOCIETY

#### DEATHS

ALEXANDROV — Vitaly J. Alexandrov, M.D., of Rutland, died March 5. He was in his fifty-sixth year.

Dr. Alexandrov received his degree from Tufts College Medical School in 1930. He was born in Russia and graduated from the University of Moscow. He was consultant and medical director of the tuberculosis unit of Burbank

Hospital, Fitchburg, director of the Fitchburg Tuberculosis Clinic, and physician-in-charge of the Rutland Cottage Sanitarium. He was director of the Northern Worcester County Public Health Association. He was a fellow of the American College of Chest Physicians, the American Trudeau Society and the American Medical Association.

His widow, two daughters and two sons survive.

BURGESS — Charles J. Burgess, M.D., of Lawrence, died February 16. He was in his seventy-seventh year.

Dr. Burgess received his degree from Tufts College Medical School in 1898. He was a member of the Roentgen Ray Society and the Radiological Society of North America, Incorporated, and a fellow of the American Medical Association.

His widow survives.

SCENNA — Donato T. Scenna, M.D., of Melrose, died March 3. He was in his forty-second year.

Dr. Scenna received his degree from Tufts College Medical School in 1930.

His widow survives.

### MEDICOLEGAL ABSTRACT

**Regulation of Practice by Government Power of government.** The plaintiff was incorporated as a nonprofit corporation. The corporation had three classes of members: administrators, practicing physicians and beneficiary members, who on pay-

ment of monthly dues, were entitled to the professional services of the participating physicians. It was provided that all compensation for doctors would be on a pro rata basis out of monthly dues. The corporation had about 5000 members in the second class and about 100,000 members in the third class, the latter was growing at a rate of 1500 members a month.

The plaintiff brought an action for a declaratory judgment to determine whether it was engaged in an illegal corporate practice of medicine and whether its activities were in the nature of disability insurance subject to certain sections of the insurance code.

On the first question, the California Supreme Court held that the prohibition against the corporate practice of medicine does not apply to nonprofit organizations. (The same doctrine has recently been expressed by way of implication in Texas where the court said by way of dictum that a corporation organized for profit cannot practice medicine and that a license to practice will issue only to a natural person — *Woodson v. Scott and White Hospital*, 186 S W [2d] 720, 1945, Texas).

On the second issue, the California court went into considerable detail in finding that the plan set forth did not constitute insurance. It found the group medical plan analogous to a consumer co-operative, saying in part:

Neither as between the corporation and the physician, nor as between the physician and the subscriber, is the compensation or any other element of the arrangement between them affected by any contingency, hazard or risk.

The latter [insurance companies] are concerned primarily, if not exclusively, with risk and the consequences of its descent, not with service or its extension in kind, quantity or distribution, with the unusual occurrence, not the daily routine of living. Hazard is predominant. On the other hand, the co-operative is concerned principally with getting service rendered to its members and doing so at lower prices made possible by quantity purchasing and economies in operation. Its primary purpose is to reduce cost rather than the risk of medical care, to broaden service to the individual in kind and quantity, to enlarge the number receiving it \* \* \* not except incidentally \* \* \* to indemnify for cost after the service is rendered.

In 1941 the plaintiff entered into a contract with the Federal Farm Security Administration to furnish medical services and hospital care to rural families. The state insurance commissioner attempted to show that the contract to provide hospitalization was insurance. For procedural reasons this question was not decided. The court did, however, say that a single aspect of a plan could not be singled out for condemnation, that the plan must be looked at as a whole, even though a contract to provide hospitalization, when viewed alone, would under some circumstances be insurance — (*California Physicians Service v. Garrison*, 155 P [2d] 885, Feb 15, 1945, rehearing denied Mar 17, 1945, hearing granted Apr 12, 1945).

## NOTICES

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, April 4, at 7 15 p m in the class room of the Nurses' Residence. Dr Bertha Offenbach will speak on the subject "The Common Eye Diseases Among Children."

### TUFTS MEDICAL ALUMNI ASSOCIATION

The annual dinner meeting of the Tufts Medical Alumni Association will be held on Wednesday, April 10, at Somerset Hotel, Boston. The committee on arrangements consists of Drs George W Holmes, Alton S Pope, Samuel Robins, A Warren Stearns, John J Todd, Edwin T Wyn and Harry Blotner.

The guest speaker will be Major General Norman T Kinnison who will speak on the subject "American Medicine in World War II." A message will be read from President Harry Truman. Other speakers will include Dr Reginald F. president of the Massachusetts Medical Society, Dr Warren Stearns and Dr Dwight O'Hara, Dr A K Packer, professor of obstetrics, Dr Louis E Phaneuf, professor of gynecology, Dr Benjamin Sachs, professor of ophthalmology, and Dr Leonard Carmichael, president of Tufts College. William E Browne, professor of clinical surgery, will present.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MARCH 28

#### FRIDAY, MARCH 29

- \*9 00-10 00 a m Some Aspects of Military Orthopedics Applied to Civilian Practice. Dr Joseph S Barr. Joseph H Pratt. Diagnostic Hospital.
- \*10 00 a m-12 00 m Medical Staff Rounds. Peter Bent Brigham Hospital.
- 10 50 a m Virus Diseases of the Skin. Dr George E Morris (Postgraduate Clinic in Dermatology and Syphilology). Amphitheater Dowling Building, Boston City Hospital.

#### MONDAY, APRIL 1

- \*12 00 m-1 00 p m Clinicopathological Conference. Peter Bent Brigham Hospital.

#### TUESDAY, APRIL 2

- \*12 15-1 15 p m Clinicorontogenological Conference. Peter Bent Brigham Hospital.

#### WEDNESDAY, APRIL 3

- \*10 30-11 30 a m Medical Clinic. Isolation Building Amphitheater Children's Hospital.
- \*12 00 m Clinicopathological Conference (Children's Hospital). Amphitheater Peter Bent Brigham Hospital.
- \*2 30-4 00 p m Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater Children's Hospital.

\*Open to the medical profession.

JANUARY 7-APRIL 22, 1946 Metropolitan State Hospital. Eleventh postgraduate seminar in neurology and psychiatry. Page 314, issue of September 6.

FEBRUARY 4-MARCH 29 Health Education Institute. Page 746, issue of December 13.

MARCH 15-SEPTEMBER 15 Boston University Course for Discharge Medical Officers. Page 240, issue of February 14.

MARCH 25-27 Medical Library Association. Page 356, issue of March 7.

APRIL 1-JUNE 1 Intensive Course in Ophthalmology. Page 240, issue of February 14.

APRIL 4 Hermann M Biggs Memorial Lecture. Page 206, issue of February 7.

APRIL 4 New England Hospital for Women and Children. Notice above.

APRIL 10 Tufts Medical Alumni Association. Notice above.

APRIL 11 Breast Tumors. Problems of diagnosis and treatment. Dr Joseph Tartakoff. Pentucket Association of Physicians. 8 30 p m. Haverhill.

MAY 6-11 American Board of Obstetrics and Gynecology. General oral and pathological examinations. Palmer House. Chicago.

MAY 13-17 American College of Physicians. Page 798, issue of December 20.

JUNE 20-22 American Association for the Study of Goiter. Page 312, issue of February 28.

### DISTRICT MEDICAL SOCIETY WORCESTER

- APRIL 10 Hahnemann Hospital.
- MAY 8 Annual meeting.

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## PSYCHOSOMATIC BACKACHE\*

MAJOR MORGAN SARGENT, M C, A U S †

**A**LTHOUGH in most discussions of backache there has been a tendency to stress the pathologic conditions that are present,<sup>1</sup> yet the fact that the symptoms may exist without definite disease or deformities is undoubtedly recognized by all who must deal with the problem.<sup>2</sup> In this paper, however, it is desired to suggest that the differential diagnosis of backache is incomplete without the consideration of psychogenic factors, for the latter are important not only as causes but also as contributing factors in cases of organic disease. The symptom of backache, like that of headache, is difficult to evaluate, and at times constitutes a minor form of malingering. Because of its frequency, particularly in military personnel, the symptom is often dismissed after casual and brief examination.

Backache is a relatively frequent complaint among patients suffering from anxiety states. An unusual opportunity has arisen in an Army Air Forces convalescent hospital, in which the primary mission is the treatment of cases of severe anxiety states, to examine large numbers of patients suffering from neurotic symptoms and incidentally complaining of backache.

These patients are for the most part men who have returned from combat tours in all parts of the world, and who on admission are suffering from symptoms of nervousness, insomnia, tension, irritability, restlessness, depression, startle reactions and other neurotic complaints. The causation and treatment of these conditions have been thoroughly described by Grinker and Spiegel.<sup>3</sup> Most of these patients are former members of air crews. A few who are not fliers have had long periods of general duty in distant theaters. Their symptoms have been brought on by long separation from home, privation, loneliness and difficult climatic conditions. No patients have been seen in whom backache was the only complaint.

The patients complaining of backache seen in this hospital fall, with considerable overlapping, into three main groups. In the first group are those in whom definite organic disease is found. It has been the policy when dealing with backache to rule out every possible organic cause by careful

clinical examination, x-ray and laboratory studies and, when indicated, additional orthopedic consultation at a nearby Army Air Forces regional station hospital. The proportion of cases in which organic disease alone has been found is less than 4 per cent. The treatment of these cases is primarily an orthopedic problem, and as such has been handled separately from the psychiatric problem. In the second group are the cases with hysterical conversion symptoms. In this classification are included patients of two categories—those suffering from what is considered to be a simple hysterical conversion symptom, and those who have in the past had some evidence of organic disease and at the time of admission appear to be exaggerating their complaints or to have had excessive prolongation of symptoms. Few if any of the patients were thought to have symptoms of a purely hysterical conversion. Practically all those in this group gave a history of some previous injury to the back, often incurred many years previously, and the point of interest is that although many of them had had absolutely no difficulty for many years, they again developed symptoms concomitant with the onset of stress in their Army life.

The following case is illustrative of the way in which the nervous symptoms are held in check by the conversion symptoms. This patient had fallen down some steps twelve years previously, landing on the base of the spine. He believed that this had caused a permanent injury, and said that for the last three or four years he had had an intermittent low backache. On examination he complained of slight pain in the region of the lumbosacral joint on backward bending, but the examination was otherwise negative. X-ray examination of the lumbosacral spine and pelvis showed a small spina bifida occulta of the fifth lumbar vertebra but was otherwise negative. The patient made the interesting and wholly spontaneous statement that when his backache disappeared he experienced extreme anxiety.

Many other patients sustained injuries during combat that were followed by prolonged persistence of symptoms. In a typical case of this kind, the patient complained of backache in the lower dorsal and upper lumbar region, which took the form of

\*From the Army Air Forces Convalescent Hospital (Don Co-Sar) St. Petersburg, Florida.

†Associate surgeon, Quincy City Hospital (on leave of absence).



a dull ache most of the time and was aggravated by exercise and fatigue. On March 18, 1944, he was thrown against a tree by a bomb explosion, was said to have had fractures of the spine and was placed in a body cast for three months. On removal of the cast he was given a back brace, which he wore for the next nine months, although he felt little benefit from it. Since the injury he had been extremely nervous, and he told the examiner that his back bothered him most when he was "nervous." After his return to this country through medical channels, he was kept in various hospitals. Although his back was x-rayed many times, all available reports were completely negative and showed no evidence of old injuries. Examination in this hospital revealed slightly increased prominence of the spinous process of the eighth dorsal vertebra and tenderness over the spinous processes of the lower dorsal and upper lumbar vertebrae. There was considerable spasm of the paravertebral muscles, particularly on the right. Motions of the back were entirely normal. Treatment consisted of psychotherapy and exercises for the back, and the brace was discarded. The back symptoms improved somewhat, but the patient was eventually discharged from the Army on the basis of a severe anxiety reaction. His nervous symptoms had begun at the time of injury. It was impossible to find out what had happened to the patient's back at the time of the blast, since the accident occurred at an outlying base in the jungle and no records were sent with the patient. One can only surmise from the x-ray reports taken after removal of the cast either that there had been no actual fractures or that, if present, they were not too severe and healed without residual evidence. This patient was treated as a physical invalid for a year, during which time he tended to exhibit exaggerated symptoms. He also showed symptoms of backache due to muscular tension.

Another patient showing conversion symptoms was injured in a crash landing in July, 1944, being struck in the lower back by a piece of metal, which caused a contusion. After having his back strapped by his flight surgeon, he continued flying. In the following month, he was shot down, captured and interned in a neutral country, where he received no specific treatment. Since that time he had had a dull ache in the lower back, which after long standing or sitting extended up the paravertebral muscles. Examination at this hospital revealed diffuse and moderate tenderness in the lumbosacral area and over the lower sacrospinalis muscle groups, with moderate spasm of the muscles of the lower back. X-ray examination of the spine and pelvis showed slight roughening of the apophyseal articulations of the fifth lumbar and first sacral vertebrae, particularly on the left. Because of these findings, physiotherapy was given in the form of baking with infra-red rays and massage, but with no relief

of symptoms. Approximately one month after entering the hospital, the patient developed symptoms of acute appendicitis, and appendectomy was performed under spinal anesthesia. Throughout the operation the patient complained of pain in the lumbosacral area, and at its conclusion this complaint was investigated. The anesthesia, which had been completely satisfactory throughout the operation, was complete at least as high as the ninth dorsal vertebra, but the patient said that he still had an aching pain in the region of the lumbosacral joint. This was obviously impossible on a somatic basis. The symptoms exhibited were considered out of proportion to the extent of the injury, but the x-ray findings, although somewhat questionable, led us to give him the benefit of the doubt, and for several weeks it was believed that he had good reason for the discomfort. Incidentally, the backache improved considerably during the course of psychotherapeutic interviews.

Even superficial psychiatric examinations revealed that the patients whose backache was thought to be mostly a conversion symptom showed comparatively fewer symptoms of overt anxiety and nervousness. Practically all the patients in this group were enlisted men, and taken collectively they appeared to be somewhat less anxious than their associates. The fact that they were enlisted men is significant only in that the level of education of the group as a whole is lower than that of the officers.

By far the largest number of patients with backache fall into the third group of cases, which are considered functional in type, the backache being due to muscular tension, the somatic manifestation of increased nervous tension. These patients exhibited all the symptoms associated with operational fatigue. As a rule they were tense and nervous, complained of insomnia and combat dreams, and found it difficult to sit still for any length of time. The more restless they were, the severer the backache was. Most of them complained of aching pain in the lower lumbar or lumbosacral region, but others located their pain in the lower dorsal area and a few described it as in the upper dorsal or posterior cervical area. The backache is usually intermittent. The pain may not be felt for hours or even days, and it is most frequently complained of at night, early in the morning and after exercise or long standing or sitting. Although in the less acute cases an increase in muscular tension is not always demonstrable, in the severer cases it can be easily elicited by palpation, particularly in the sacrospinalis and erector spinae muscle groups, and at times the muscles go into almost boardlike spasms. Several patients have been seen in whom the back muscles were under such tension, even in a relaxed position, that fibrillary contractions were visible. These patients exhibit signs and symptoms of easy muscular fatigue, which is easily

noticeable among the severe cases and is partly proved by the poor showings made during tests of physical fitness. Consequently, it is believed that increased tension of muscles that are easily fatigued tends to cause symptoms far more easily than it does in more normal muscles. When demonstrable tension is present by palpation, there is often some limitation of forward bending, with an increase in pain, and there is some pain on straight leg raising and also on forward tilting of the pelvis with both flexed knees brought up toward the chest.

The signs and symptoms often vary in the same patient from day to day, as one would expect when the muscular tension is the result of nervous tension. Many of these patients have considerable difficulty in sleeping, and when once asleep they have combat and anxiety dreams that keep them tense and restless throughout the night. This is apparently the reason why so many patients complain of backache during the night and on awakening in the morning. The inability of the muscles to secure rest results in a constant state of fatigue, and it is small wonder that any additional burden placed on them by exercise or by long use in the maintenance of posture results in protest, which is manifested by pain and aches.

In contrast with the patients suffering from backache due to organic causes and with those with conversion symptoms, almost all patients with backache due to muscular tension complain of a rather diffuse ache, which they can localize only in the general region of the back. A large number of these patients attribute the onset of symptoms to some injury, but as a rule the injury is known not to have been severe, and at times evidence of it is almost nonexistent. This is illustrated by a patient who first noticed low lumbar backache in October, 1944, which developed after a burst of flak beneath the ball turret in which he was riding. At that time he was not injured, either by the flak or by concussion. On his admission to this hospital five months later, after completion of his combat tour, he complained of low lumbar backache, usually coming on in the morning, wearing off during the day and coming on again toward the evening. Examination of the back revealed an extreme degree of tension in the sacrospinalis muscle groups. X-ray examination of the lumbosacral spine was negative, and at the time of examination it was thought that the backache was a purely psychosomatic symptom due to muscular tension.

Another patient stated that off and on for fifteen years he had suffered low-back pain, which came on at times of excitement. He noticed this particularly while flying and when in a tight spot. There was no history of any injury. Examination revealed only marked spasm of both sacrospinalis groups.

Considerable difficulty exists in the correct evaluation of cases when the main problem seems to be muscular tension but careful examination reveals

some organic finding that may contribute to the picture. A typical case is that of a patient who suffered an injury to the lower back in December, 1943, when his plane was ditched. After a short period of disability he had little trouble until August, 1944, when he struck his back and strained it severely on falling from a catwalk into the bomb bay of a B-17. Since then he had had lumbar backache, present mostly when exercising. Examination of the back revealed moderate diffuse tenderness in the lumbosacral region and over the lower lumbar muscles. There was no postural deformity, and x-ray films of the spine were negative. Complaints of back pain continued and were greatly aggravated by a train ride while on furlough. It was believed that the patient might have chronic low-back strain but that most of the symptoms were psychosomatic in origin.

Another example of this type of patient is one who complained of low lumbar backache that first came on during his combat mission. There was no history of injury. On several occasions clinical examinations revealed nothing abnormal, but the patient said that his back ached most in the morning and late evening. X-ray examination showed some roughening between the apophyseal articulations of the fourth and fifth lumbar vertebrae. This was taken into account, but it was thought that the symptoms were due to muscular tension, which probably aggravated and perhaps made symptomatic the organic disease.

The pain in a great many of these cases is closely similar to that produced by protective muscle spasm in injuries of the lower back. Indeed, it is often of the same type, since it is generally believed that the pain of protective muscle spasm is caused by the persistent pull of muscles on their periosteal attachments. Therefore, in cases in which an injury such as a muscular or ligamentous sprain or strain has occurred within a period of eight to twelve weeks, one cannot say with any degree of certainty that the discomfort is not entirely of organic origin. In our opinion, however, without proved organic disease sufficient to cause it, the prolongation of such pain for several months is generally indicative of muscular tension arising from some other cause, presumably increased nervous tension.

Many cases have been encountered in which backache was undoubtedly due solely to tension, and in most of these cases the pain disappeared after a brief period of psychotherapy for the anxiety state. The discomfort of those with concomitant organic disease is often greatly relieved, but even with the combination of psychotherapy and orthopedic treatment the results are, quite understandably, not entirely satisfactory in all cases.

The treatment of patients with backache due to conversion symptoms or caused by increased muscu-

lar tension must of necessity be primarily psychiatric. In patients with conversion symptoms, it has been found by experience that attempts to deal with the problem by means of physiotherapy, injections of novocain and medical measures tends to focus the patient's attention on the symptom and, if anything, to cause it to become fixed. The same thing is also true, perhaps to a lesser extent, of patients with backache due to muscular tension. Physical and medical procedures are only palliative. Physiotherapy can be carried on for weeks with temporary relief of discomfort for one or two hours after a treatment, or perhaps a little longer, but the symptoms invariably recur. Because of this, we believe that physiotherapy should be reserved for selected cases, usually those with definite organic difficulties, and that it should not be used for cases with conversion or purely tension symptoms. In this hospital the efforts of the Surgical Department to co-operate with the Neuropsychiatric Department have met with considerable success. These results have been accomplished, first, by ruling out the organic difficulties and reassuring the patient that nothing is being overlooked in the attempt to track down the cause of his symptoms, and, second, in preparing the patient for the full benefit of psychotherapy by endeavoring to explain to him in simple terms some of the causes of his backache.

Most of the patients with backache due to muscular tension reveal at some time during their examination the presence of some nervous symptoms, and a little careful questioning leads them to admit that they are more tense than they were previously. In this hospital, where the patients frequently climb upstairs to the various wards, they remark that their legs seem to tire considerably faster than previously or admit to easy muscular fatigue while engaging in exercise. Most of these patients also state that they have noticed an increase in general muscular tension in one form or another and that they find it difficult to relax. When these points have been demonstrated and the patients have perceived that they apply to themselves, it is pointed out to them that increased nervous tension causes increased muscular tension, and that since the muscles under such tension are seldom given a chance to relax as they would normally do, they are in a state of chronic fatigue, consequently, the

patients tire much more easily than usual when subjected to additional stress in the form of exercise, or even in the maintenance of posture when merely sitting or standing. Whether this is always the case may be debatable, but at least the point is understood by the lay mind. The fact that combat and anxiety dreams at night also cause much muscular tension is readily understood by those who experience them. With this brief explanation of the mechanisms involved, the patients are told that whereas they can be given temporary relief by such measures as heat and massage, this treatment is only temporary, and that the way to get permanent relief is to be relieved of the basic nervous tension. They are assured that this can be done by co-operation with the psychiatrist. In some patients this type of explanation seems to be sufficient in itself to cause a considerable decrease in symptoms, and in the majority it is believed that the way is paved for beneficial therapy of the primary condition by the psychiatrist.

#### SUMMARY

Backache is a frequent complaint among persons with anxiety states.

In a hospital where large numbers of men with anxiety states have been seen, the type of backache observed is due in most cases to hysterical conversion symptoms or to functional backache caused by muscular tension and fatigue. The latter type of backache is by far the most frequent one, but the two types are often associated.

Backaches caused by muscular tension and fatigue improve when the anxiety state is relieved by psychiatric treatment.

It is believed that pain of psychogenic origin should receive careful consideration in the differential diagnosis of any case of backache, especially since it may be closely associated with backache caused by organic disease and is often the cause of the prolongation of symptoms.

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## THE USE OF PHTHALYLSULFATHIAZOLE (SULFATHALIDINE) IN COLONIC SURGERY\*

ROBERT THOMSON, M D,† AND ERNEST M DALAND, M D ‡

BOSTON

IN 1941, Poth and Knotts<sup>1</sup> introduced succinylsulfathiazole (sulfasuxidine) as an intestinal antiseptic and bacteriostatic agent. It has proved especially valuable as an adjunct to surgery of the large bowel, as well as in the treatment of certain medical conditions. A further improvement was made in this field with the discovery of phthalylsulfathiazole (sulfathalidine§) by Poth and Ross<sup>2</sup> in 1943. This new drug has the advantage of having twice the bacteriostatic activity of succinylsulfathiazole but requiring only half to one third of its dosage. In addition, the drug has not given rise to any toxic reactions such as have occasionally been seen with succinylsulfathiazole. Mattis et al,<sup>3</sup> in extensive toxicologic studies on the effect of phthalylsulfathiazole in mice, rats and monkeys, reported no toxic manifestations in spite of large doses administered orally every four hours for thirty days. They found extremely low blood concentrations of free and total sulfathiazole, which they attributed to retention in the gastrointestinal tract of all but small amounts of the drug, the small amount that was absorbed was rapidly excreted by the kidneys. Our studies of the blood and urine concentrations of this drug are in agreement with the findings of these investigators. Furthermore, phthalylsulfathiazole is effective in the presence of diarrhea or in patients who are receiving purgatives, whereas the effectiveness of succinylsulfathiazole under these conditions is greatly reduced.

The stools following the use of phthalylsulfathiazole are solid and retain some of their odor, as opposed to the odorless, semifluid movements that occur after the giving of succinylsulfathiazole. The exact mode of action of these drugs is not yet clearly understood. The chemical and bacteriostatic properties of phthalylsulfathiazole have been studied and reported by Poth and Ross.<sup>4</sup>

In this paper we are reporting our experience with the new drug at the Pondville Hospital, where it has been used in connection with surgery of the large bowel. It has been employed in the preoperative preparation of 51 unselected cases over a period of fifteen months. It has also been used in 12 cases of nonspecific gastroenteritis with diarrhea, in which it has apparently been of definite benefit. Our studies of the blood and urine concentrations of this

drug are in agreement with the findings of the above investigators.

The type of case in which phthalylsulfathiazole was used is shown in Table 1. In several of the cases the drug was used more than once, when the operation was done in stages. There was no evidence in any case of sensitivity to the preparation.

In Table 2 are shown the types of operation performed. There were 3 cases in the group given

TABLE 1 Cases in Which Phthalylsulfathiazole Was Employed

DIAGNOSIS	No. of Cases
Carcinoma of rectum	30
Carcinoma of left colon and rectosigmoid	13
Carcinoma of right colon	4
Carcinoma of transverse colon	1
Tumor of rectovaginal septum	1
Polyposis of large bowel	1
Carcinoma of urinary bladder	1
Total	51

routine preoperative doses of phthalylsulfathiazole in which the patients subsequently refused operation or in which it was considered inadvisable. The administration of the drug was stopped on the morning of operation and was not continued postoperatively in all cases except 1, in which a tumor of the rectovaginal septum was removed. The rectum was opened and repaired during operation, and it was decided to continue the drug. Convalescence was uncomplicated.

In cases of resection of a blind loop of bowel or second-stage posterior excision of the rectum, daily preoperative irrigations with a suspension of

TABLE 2 Types of Operation Performed

OPERATION	No. of Cases
Abdominoperineal resection	
One-stage	12
Two-stage	2
Resection of tumor, transverse and descending colon and rectosigmoid with primary anastomosis	9
Palliative colostomy	9
Colostomy revision	5
Right colectomy	
One-stage	3
Two-stage	1
Colostomy or enterostomy closure	1
Uterointestinal anastomosis	2
Resection of blind loop of bowel	2
Enterocenterostomy	1
Excision of tumor of rectovaginal septum	1
Total	49

phthalylsulfathiazole were given. Of the 9 patients who received resection of tumors of the transverse, descending or rectosigmoid colon, 4 had a preliminary or complementary cecostomy, 4 had Miller-Abbott tube decompression, and 1 had neither. In none of these cases was there any serious postoperative distention.

\*From the Pondville Hospital (Massachusetts Department of Public Health) Walpole, Massachusetts.

†Formerly chief resident, Pondville Hospital.

‡Instructor in surgery Harvard Medical School, chief-of-staff Pondville Hospital, visiting surgeon Massachusetts General Hospital.

§The material for this study was supplied by Sharp and Dohme Incorporated Philadelphia.

### Dosage and Preoperative Preparation

The routine procedure has been to place these patients on a low-residue diet and to begin the administration of phthalylsulfathiazole five or six days before operation. Giving the drug for shorter periods of time preoperatively proved unsatisfactory. It has, however, been given in full dosage for as long as fourteen days without any ill effect. The initial dose is 0.05 gm per kilogram of body weight, or between 2.5 and 4.5 gm for most patients. Following this, 1 gm (two tablets) is given every four hours day and night. Enemas are used preoperatively when indicated, strong purgatives are not employed. Whole blood, plasma and amino acid preparations are used as indicated in the correction of anemia and low serum protein. For twenty-four hours be-

### Laboratory Data

Determinations of the blood and urine levels of phthalylsulfathiazole were made daily, as well as red-cell counts, white-cell counts and hemoglobin determinations, in the 19 cases listed in Table 3. No facilities were available for bacteriologic examination of the stools. Such studies have, however, been reported by Poth and Ross,<sup>5</sup> and the effectiveness of phthalylsulfathiazole in reducing coliform and other organisms has been well established.

In Table 3, it will be noted that the daily dose as well as the number of doses varied, this was due to the fact that in these cases an attempt was made to adjust the dosage as accurately as possible to the patient's weight. In view, however, of the extremely

TABLE 3 Blood and Urine Concentrations of Phthalylsulfathiazole as Sulfathiazole

CASE No.	DAILY DOSE gm	No OF DOSES DAILY	AVERAGE BLOOD CONCENTRATION		AVERAGE URINE CONCENTRATION	
			FREE mg /100 cc	CONJUGATED mg /100 cc	FREE mg /100 cc	CONJUGATED mg /100 cc
1	4.5	6	0.13	0.54	8.8	31.1
2	3.0	6	0.31	0.17	1.2	1.9
3	2.5	5	0.04	0.28	2.5	4.6
4	2.5	5	0.24	0.40	3.5	10.0
5	3.0	6	0.23	0.59	10.7	17.5
6	3.0	6	0.15	0.31	2.3	6.0
7	3.0	6	0.28	0.41	1.5	4.0
8	3.0	6	2.04	2.22	5.8	12.9
9	3.0	6	0.08	0.60	3.6	7.1
10	2.5	5	0.09	0.20	1.4	2.9
11	3.0	6	0.13	0.31	3.9	11.0
12	4.0	4	0.08	0.18	5.2	13.9
13	3.0	6	0.68	0.81	11.9	32.6
14	3.5	6	2.68	14.14	19.6	36.8
15	2.5	5	0.14	0.26	2.9	8.6
16	3.0	6	0.19	0.20	14.1	26.9
17	3.0	5	0.24	0.41	3.6	12.8
18	2.5	5	0.52	0.78	8.4	21.6
19	3.0	6	0.18	0.58	12.3	36.6

fore surgery the patient is given only clear liquids by mouth, and routine doses of sulfadiazine are administered during this period, either by mouth or intravenously.

At the time of operation, in all cases except 1 in which there was no obstruction, the bowel was found to be well cleaned out and free from distention. The exception was a case of unobstructed carcinoma of the rectum in which abdominoperineal resection was carried out after the patient had received phthalylsulfathiazole for only three days. In only 1 case, mentioned above, was the drug continued postoperatively, but it is thought that in many cases such continuation could and should be carried out. In support of this may be cited the case of a seventy-eight-year-old man in which a combined abdominoperineal resection was done in one stage after routine preparation. Four days postoperatively the end colostomy slipped back into the peritoneal cavity. The bowel was then retrieved and sutured to the abdominal wall. There was undoubted soiling of the peritoneal cavity, but the patient did not develop peritonitis. He was eventually discharged in a satisfactory condition.

low blood concentrations of the drug (measured as sulfathiazole) and in the absence of any toxic manifestations, the simpler routine was thereafter adopted of giving all patients 1 gm every four hours after the initial dose. In Cases 8 and 14, it will be noted that the blood level was appreciably higher than that in any other case, reaching levels of free drug of 2.040 and 2.681 mg per 100 cc, respectively. This is due to the fact that these patients were inadvertently given routine doses of sulfadiazine by mouth eighteen to twenty-four hours before these determinations were made.\* The figures are interesting in that they show how little phthalylsulfathiazole is absorbed by the blood stream as compared with sulfadiazine.

### Results

There were no toxic reactions from phthalylsulfathiazole in this series.

Among the 49 operative cases — fifty-two operations — in which phthalylsulfathiazole was used,

\*The routine preoperative use of sulfadiazine as outlined in the section on preoperative preparation was not begun until after the data of the first 19 cases (Table 3) had been collected.

there were 4 cases (8 per cent) with infection. Three patients had wound infection and 1 developed generalized peritonitis and died, a mortality rate of 2 per cent. One of the patients with wound infection received an abdominoperineal resection. The end colostomy slipped back below the peritoneal floor on the fifth postoperative day, but it was almost immediately retrieved, and no peritonitis ensued. A similar accident occurred in another case in which wound infection developed, the mishap was not detected for eight to twelve hours. Colostomy was revised and the patient recovered. These 2 patients had received the drug for four and ten days, respectively, before operation.

The single operative fatality in this group occurred in a patient who had a two-stage operation for carcinoma of the splenic flexure. Following cecostomy, the patient received sulfathiazole for eight days before the second stage of the operation. Extension of the tumor necessitated partial resection of the stomach and splenectomy, as well as resection of the splenic flexure with primary anastomosis. The patient died three weeks postoperatively of peri-

tonitis. The effectiveness of the drug in this case was probably somewhat diminished by the presence of the cecostomy.

### SUMMARY

Phthalylsulfathiazole, a new intestinal antiseptic and bacteriostatic agent, after its use in 51 cases was ranked as of definite value as an aid in surgery of the large bowel. Its small dosage, great bacteriostatic activity and low toxicity make it an easy, effective and safe drug to use. Continued use of the drug postoperatively, wherever possible, is advised.

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## CHRONIC DISABILITY IN MILD CASES OF TRENCH FOOT

MAJOR FRANKLIN K. PADDOCK, M C, A U S

**R**ELATIVELY little study has been made of the persistent signs and symptoms of trench foot and immersion foot, most papers on this disorder dealing with their acute manifestations.<sup>1, 2</sup> According to my experience, however, these symptoms may be disabling for at least one year and are apparently not alleviated by any of a variety of therapeutic measures, including psychiatric treatment. At the present time, with relatively large numbers of patients with this condition awaiting disposition at military hospitals in this country, such a study appears timely.

During February and March, 1945, in Italy, an opportunity was presented to study with special attention some of the manifestations of the later stages of trench foot. These cases, all of which were contracted in the Apennine Mountains of Italy during the winter of 1944-1945, were of mild to moderate severity and were on the whole less severe than those encountered during the preceding Italian winter campaign.

Since the later manifestations of trench foot are typified by subjective complaints most difficult to evaluate, an attempt was made to determine what abnormal responses, if any, could be elicited by various stimuli. In the cases studied, within one or two months after onset, the acute manifestations of edema and gangrene or pseudogangrene had disappeared and spontaneous pain, with tenderness of

the soles of the feet, was the chief complaint. The persisting disturbances fell into two main groups — the vascular type, characterized by a tendency to coldness and cyanosis of the feet, and the neural type, marked by pain on firm pressure over the soles of the feet, superficial hypalgesia, loss of proprioception, diminution of temperature discrimination, hyperhidrosis and poor toe-flexion ability.

### VASCULAR DISTURBANCES

It is a frequent observation that patients suffering from the later stages of trench foot tend to have cold, sweaty feet that on dependency rapidly develop cyanosis. The following conclusions were reached from studies of this tendency.

When the shoes and socks of patients with trench foot are removed, the feet are found to be devoid of cyanosis, whether the patients have been stationary or moving about and even though the toe-skin temperatures are usually low (20° to 23°C). On dependency without the constricting shoes and socks, however, cyanosis generally develops within five minutes. It can be made to disappear by elevating the feet, a normal pink color taking its place. Furthermore, on elevation the cyanotic hue can be readily milked out of the toes. If a uniform light-pressure bandage is applied to a toe when it is pink and the foot is placed in a dependent position, the bound toe is seen to be pink immedi-

ately following the removal of the bandage, even though the remaining toes have become cyanotic. When the foot vessels, either by direct or by reflex methods, have been brought toward full dilatation, as shown by a skin temperature of 30°C or higher, cyanosis does not appear on dependency so long as vasodilatation, as shown by the skin temperature, persists. With the return of vasoconstriction and cooling of the skin cyanosis develops. If the cyanotic toes are examined through a capillary microscope, it is found that gentle pressure with a glass slide eliminates the cyanosis without obliterating the visible capillaries.

An attempt was made to elicit the so-called "triple response" of the superficial vessels in the distal extensor surfaces of the feet both of normal persons and of those suffering from trench foot. In both groups, the local red response with surrounding pallor was usually obtained by firm stroking with a rounded point, but no wheal or flare was observed in either group. In addition, approximately 0.1 cc of a 1:1000 solution of histamine phosphate was injected intradermally over the mesial aspect of the first metatarsophalangeal joint of 2 normal persons and of 4 patients with trench foot. In each case a wheal with a surrounding flare of intense erythema appeared after approximately the same interval. This effect could not be reproduced in normal feet by a similar injection of normal saline solution. In the cases of trench foot, with the feet dependent and hence cyanotic, the zone of erythema stood out strikingly against the surrounding cyanotic skin. Simultaneous release of local pressure in both the cyanotic and the erythematous areas revealed a much more rapid return of color to the latter than to the former.

During the winter of 1943-1944, unilateral lumbar sympathetic block in 17 cases of trench foot brought about a prompt rise—within a half-hour—of the skin temperature of the foot on the affected side. This observation was verified in 2 cases during this study, the toe-skin temperature on the blocked side rising to above 30°C within a half-hour, with cessation of sweating. In 1 case so treated, the intradermal injection of 0.1 cc of 1:1000 histamine phosphate solution at the bases of both big toes at the height of the vasodilatation brought out prompt wheals with surrounding flares bilaterally.

### *Effects of Local Heat*

The effects of local heat on cases of trench foot were studied by the following method. The left foot was placed in a specially constructed hot-water bath that allowed the foot to be submerged to the level of the malleoli but permitted the tip of the big toe to protrude through a rubber-lined opening so that skin temperatures could be taken. Since it was found by experiment that a minimum temperature of 39°C was necessary to bring about full vasodilatation, the bath was kept at a temperature

of 39 to 40°C by the addition of hot water. The left foot was kept in the bath until a toe-skin temperature of 30°C was obtained. When this had occurred, the foot was taken from the bath, dried and placed on a dry bath towel, and skin temperatures were taken at regular intervals for the next half-hour.

Various checks of this method were made. First, the temperature of the surrounding air was taken at regular intervals and found not to vary more than by 2 or 3°C during any single experimental period, usually being between 21 and 25°C. Secondly, the skin temperature of the right big toe was taken regularly at the same time as that of the left and was found to vary at most by 2 or 3°C. Thirdly, the skin temperature of the thumbs was taken periodically and was found to start at different levels and to vary markedly from patient to patient. No correlation, however, could be found between the temperature of the thumb and that of the left big toe. Fourthly, it was thought that the constriction of the left big toe by the rubber-lined opening might play a significant part in determining its temperature lability. Therefore in 2 cases that showed markedly delayed vasodilatation by this method, the foot was set in the hot-water bath with the water covering only the lower part of the foot, the tip of the big toe being above water level and free of constriction. The difference between the vasodilatation time obtained by this method and that obtained by the basic method was not significant. Furthermore, the factor of constriction was common to the normal controls and to the patients with trench foot thus tested. Fifthly, the skin-temperature measuring device\* showed relatively slight variations when tested against a mercury thermometer. Skin temperatures, however, did show variations of as much as 0.5°C, depending on the exact spot on the toe tip tested. An attempt was therefore made to place the filament in as nearly the same spot as possible on each occasion. Lastly, the possible effects of emotional tension on the subjects' neurovascular tone were controlled as well as possible by personal acquaintance with the subject and by reassurance.

The feet of 11 normal persons and of 12 patients with trench foot were studied by this method. In the normal persons, a maximum period of forty-six minutes was required for the skin temperature of the left big toe to reach 30°C. In the cases of trench foot, however, there was a definite trend toward a prolonged vasodilatation time, more than fifty minutes being required to achieve a skin temperature of 30°C or over in half the cases. In 3 of these cases, furthermore, the toes did not reach this degree of temperature even after having been in the water for eighty minutes. These cases with prolonged vasodilatation time showed a good cor-

\*Dermalog, manufactured by the McKesson Appliance Company, Toledo, Ohio.

relation with the tests of reflex vasodilatation (see below) in 3 out of 5 cases

When the feet were removed from the hot-water bath, no obvious differences occurred in the curves of skin temperature, which was tested over a half-hour period, between the patients and the controls

### *Reflex Effects of Heat*

The reflex effects of heat were studied by the following method. The patient was surrounded by seven towel-wrapped chemical heating pads\* — which may reach a temperature of 90°C — and was covered by six blankets. Both feet and the left hand were left uncovered. Every five minutes a recording was made of the room temperature, the oral temperature and the skin temperature of the left thumb and of both big toes. The test was considered satisfactory if the oral temperature rose by at least 1°F or a diffuse diaphoresis occurred within a half-hour period, or if both conditions obtained. If neither of these criteria was satisfied, the test was repeated on another day.

In the normal person, a skin temperature of above 30°C is said to occur in both thumbs and toes within a half-hour period. In 6 persons so tested, however, the skin temperatures of the big toes reached 30°C or higher in a maximum of forty-five minutes after the application of heat. For this reason, fifty minutes was taken as the upper limit of normal.

By this method 19 cases of trench foot were studied. In 6 of these, there was failure to reach the required skin temperature within a fifty-minute period, and in 2 of them as much as ninety-five minutes elapsed after the application of heat before this state was achieved.

\* \* \*

The results of these various observations were interpreted as demonstrating certain abnormalities in the neurovascular mechanism of trench foot. It appears that the cyanosis of the feet that develops on dependency is apparently owing to stasis of blood on the venous side of the capillary loops, presumably in the subpapillary venous plexus, and that the cyanosis can be eliminated by an increase in the venous return, effected either by increasing the blood flow through arteriolar dilatation or by increasing the venous tone through extrinsic pressure. Some evidence was also obtained that the capillaries in these relatively mild cases of trench foot are intact.

The results of both the local and the central application of heat were interpreted as showing that at least the more superficial arterioles of the distal portions of the feet have increased tone. Since the paralysis of the sympathetic ganglions regulating those vessels leads to a prompt arteriolar dilatation, it may be assumed that the apparent

vascular disturbance lies in reality in the sympathetic nervous system, possibly in the autonomic nerve endings themselves, or that the mechanism is a simple reflex vasospasm such as has been demonstrated in response to painful stimuli. The hyperhidrosis may be taken as further evidence of excessive sympathetic activity.<sup>3</sup> Furthermore, although pathological examinations of the amputated portions of the severer cases of trench and immersion foot have revealed vascular occlusions,<sup>4, 5</sup> there was no evidence in the milder type of case included in this study that any significant intravascular obstruction was present, the arterioles being able to react completely, even if slowly, to appropriate stimuli.

### NEURAL DISTURBANCES

Patients suffering from trench foot have difficulty in walking. In almost all cases this difficulty is primarily due to deep tenderness in the feet, which is most marked over the first metatarsophalangeal joint. The patient in placing his foot on the floor usually first throws his weight on the heel and then inverts his foot, so that the weight of the body as it moves forward is distributed along the lateral margin, the ball of the foot touching the ground last and only gently. The toes are generally held in a cocked-up position. The gait tends to be shuffling.

Neurologic examination of these feet in almost all cases reveals superficial hypalgesia to pinprick involving at least the flexor surface of the big toes. The more extensive areas of hypalgesia may have a narrow zone of hyperalgesia at their proximal border, and in an occasional case the superficial sensation of the whole distal portion of the foot is hyperalgesic. Hypesthesia or anesthesia to light touch is found too frequently in the toe tips of military personnel to admit comparison with cases of trench foot. Proprioception of the toes, as evidenced by position and vibration sense, may be diminished or absent. In 33 patients studied particularly for this phenomenon, 13 had poor position sense and 8 had absent vibratory sense of the big toes.

An occasional patient shows diminished or absent ability to flex the toes voluntarily. This has been noted in the earliest stages of trench foot while the patient was still bedridden. Of 33 patients with trench foot examined with this especially in mind 8 had poor toe-flexion ability. A more careful analysis of this disability indicates that the fault lies not in the short but rather the long flexor muscles, since flexion is absent in the distal rather than in the mesial or proximal phalanges. In all cases the toes could be flexed by the examiner with ease, and in most cases this caused no obvious discomfort. This disability showed no definite correlation with loss of proprioception sense but did show some correlation with the severity of the disease, being more frequent in the severer cases.

\*Kemi therm, manufactured by the National Mineral Company, Chicago



Galvanic and faradic stimulation\* of the long extensor and the long and short flexor muscles of the toes and faradic stimulation of the plantar nerve were carried out on 7 patients with trench foot, who showed diminished to absent ability to flex the toes. The same average quantity of ohms in the galvanic stimulation and of volts in the faradic stimulation brought the same threshold response in the patients with trench foot as it did in a similar number of normal persons. With these results in mind, 2 intelligent and co-operative patients with trench foot who had poor toe-flexion ability — one unilaterally — were given daily re-education in toe motion. At the end of five days both patients were able to flex the terminal phalanges of the big toes voluntarily. They had been in the hospital for sixty to ninety days at the time this experiment was tried without regaining this ability by themselves.

The ability to distinguish between hot and cold was tested. With the use of test tubes filled with warm and with cool water, with a temperature difference between them of 15 to 20° C, 21 normal persons and 14 patients with trench foot were examined, the test tubes being held for a maximum of five seconds against the area in and around the big toes. In all cases of trench foot so tested there was a loss of temperature sense in at least the tips of the big toes, whereas in the normal persons — except in 1 case complicated by marked toe callus — there was a ready ability to distinguish the temperature difference. In addition, a minority of the patients with trench foot had this loss at the base of the big toes on both the flexor and extensor surfaces. In all the cases of trench foot except 1, hypalgesia began proximal to the area of loss of temperature sensation. There seemed to be no correlation between proprioception and the extent of temperature loss, in that position sense might be present even when there was a loss of temperature sensation over the entire big toe.

An attempt was made to demonstrate the presence or absence of deep-seated sensitivity to cold in the distal portions of the foot in cases of trench foot. The subject was seated in a chair with the toes and ball of one foot and the fingers of one hand submerged in a pan of ice water. Since higher temperatures gave equivocal results in normal persons, the temperature of the water was kept at about 5°C. The members were kept submerged for a minimum of ninety seconds.

Ten patients with mild to moderate cases of trench foot and 10 normal persons were tested by this method. All the patients with trench foot complained of aching of the fingers within one minute, but only 1 complained of aching in the submerged portion of the foot. All the normal persons complained of aching of the foot, but in most cases the pain was confined to the areas of the metatarso-

phalangeal joints and was not of sufficient severity to make the subject withdraw his foot from the bath.

\* \* \*

Either loss or exaggeration of superficial pain over the more distal portions of the feet appears to be common to all cases of trench foot. Loss of proprioception may occur in some cases, but deep pain sensation tends to persist. Loss or diminution of temperature sensation is a frequent finding. Since it is said that in a cooled nerve the sense of warmth is lost before that of coldness,<sup>6</sup> it was hoped that these observations would help to distinguish between nerve damage caused by cooling and that caused by asphyxia. No conclusions in this regard, however, could be drawn.

It has been stated that the deep-seated aching due to cooling of an extremity is mediated by the small nonmyelinated nerve fibers of Class C.<sup>7</sup> The absence of this pain in cases of trench foot is evidence that these fibers are damaged. Although the above study tends to show that such damage has occurred, the method is in essence dependent on subjective interpretations of pain and hence is not particularly valuable as a test for this condition.

The loss of voluntary toe flexion found in some cases is rather difficult to understand. The motor nerves and muscles show no obvious functional or structural abnormality. It seems likely that this disability is due to a disturbed toe-flexion pattern, perhaps lost during the earliest stages of the disease, when acute edema and vascular disturbance make toe motion painful.

#### PATHOLOGY

Scattered reports of the pathology of this condition are available in the literature.<sup>4, 5</sup> In severe cases, gangrene with complete or partial vascular obstruction is obvious. Intense fibrosis and increased deposition of collagen have been described in severe cases of immersion foot.<sup>8</sup>

In 3 of the mild cases examined in this study, biopsy specimens of the tissues overlying the mesial aspect of the proximal phalanx of the big toe were taken. Microscopical examination† of sections stained with the Bodian protargol method revealed minor changes in the nerve trunks consisting of focal swelling of the axone cylinders. The nerves appeared to contain a comparatively large amount of fibrillar tissue for the location and the number of Schwann-cell nuclei. The vessels, corium and epidermis appeared normal, and there was no evidence of an increase in fibrosis or collagen or of a decrease in fat.

#### COMMENT

The chronic disability resulting from mild trench foot presents an interesting problem. In the early stages of the disease, damage to the blood vessels,

\*This was done with the technical assistance of First Lieutenant Helen T. Lawrence, physiotherapist.

†These examinations were interpreted by Major Victor N. Tompkins, M.C. A.U.S.

resulting in inflammatory edema and a tendency to gangrene, overshadows the other aspects of the condition. When this phase has subsided, the patient is left with painful, tender feet that have a tendency to become cyanosed on dependency or exposure to cold. On gross examination in a warm room with the legs horizontal, the feet appear completely normal, and only on neurologic examination of the distal portions of the feet does any abnormality become apparent. When cyanosis is induced, vascular disease is at once assumed and is considered to be responsible for the disability. From the observations in this study, however, this does not appear to be the case, rather it is the terminal nerve twigs that are at fault—a terminal neuritis. Furthermore, one occasionally encounters a supposedly normal person whose extremities become cyanotic under similar conditions but who does not complain of any pain or tenderness such as that experienced by patients with trench foot. It is because neuritis is the underlying fault that, at least in my experience, interruption of the sympathetic pathways to the feet does not bring about frank relief of the symptoms, although it relieves the cyanotic tendency—and, of course, the associated hyperhidrosis.

On the basis of prolonged observation of these patients in the Mediterranean Theater of Operations, it has been found that the complaints of pain and tenderness clear extremely slowly. During the summer, hyperhidrosis, with resultant skin maceration and a tendency to epidermophytosis, was frequent. The pain and tenderness felt on walking was less during the warm weather, but even so prevented the sufferer from taking long marches. During the subsequent winter, a year after the onset of the disease, when the weather was cold and damp, spontaneous aching occurred and was associated with further diminution of walking ability, although not to its initial levels. It appears likely that this disability will disappear only after a period

of years and that therapy directed at the blood vessels and non-neural tissues will be of no avail.

#### SUMMARY AND CONCLUSIONS

A study was made of the later manifestations of trench foot of relatively mild severity.

A variety of related observations of the arterioles, capillaries and venules revealed that there was increased arteriolar tone, apparently secondary to increased sympathetic stimulation, but no evidence of arteriolar obstruction. The capillaries and venules were apparently normal.

Observations of the sensory and motor nerve disturbances revealed that besides superficial hypalgesia there was frequently diminution of temperature, vibration and position sense. Poor toe-flexion ability was shown to be owing to no obvious structural abnormality. Deep-seated sensitivity to cold tended to be absent.

The lesions of the less severe cases of trench foot are conceived of as involving all the more superficial foot tissues, but with a quantitative variation from patient to patient as regards the tissues affected. It appears that the disability encountered in the later stages of mild cases of this condition are more dependent on neural than on vascular disease. Microscopic examination of the damaged tissues tends to confirm this concept.

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## HEMORRHAGE FROM THE GALL BLADDER\*

PERRY B HUDSON, M D,† AND PEER P JOHNSON, M D ‡

BEVERLY, MASSACHUSETTS

THE purpose of this paper is twofold—to present 4 cases of hemorrhage into or from the gall bladder, 3 of which had unusual features, and to show the significance of hemorrhage into the gastrointestinal tract in cases of cholelithiasis, as indicated by routine examination of the stools

Of the cases of massive hemorrhage from the gall bladder, 1 was due to neoplasm, so that the hemorrhage was not remarkable. The other 3 cases, however, are similar to the 24 already contained in the literature. This condition was first reported in 1892 by Naunyn,<sup>1</sup> who described 3 cases of ruptured arterial aneurysms causing massive hemorrhage into the gall bladder. In 1903, Huguenin<sup>2</sup> reported a case of such a hemorrhage into the gall bladder and throughout the extrahepatic biliary duct system, but this was found to have been caused by carcinoma of the common duct. In 1915, Schnyder<sup>3</sup> reviewed the literature and found 8 cases similar to those presented here, and added 2 of his own. In 1925, Heusser<sup>4</sup> reported the case of a forty-seven-year-old man with cholelithiasis who developed massive hemorrhage into the lumen of the gall bladder. Perhaps the most remarkable case contained in the literature is that given by Fiessinger et al.<sup>5</sup> His patient was a four-year-old child who developed massive idiopathic bleeding from a noninfected gall bladder that contained no stones. In 1939, Meyer-May<sup>6</sup> reported a case of enormous hemorrhage into the gall bladder that was probably due to trauma incurred in a football game.

Another group of hematocholecysts found in the literature are those reported by Leared<sup>7</sup> in 1858, Schnyder<sup>3</sup> in 1915, Gjellerup<sup>8</sup> in 1921, Waters<sup>9</sup> in 1926, Bartlett and Bartlett<sup>10</sup> in 1936 and Mailer<sup>11</sup> in 1939. In all these cases there was spontaneous rupture of the gall bladder, with considerable free intraperitoneal hemorrhage. Each case represented a mechanical tearing of the wall of the gall bladder secondary to blockage of the cystic duct. These cases, together with those of traumatic hemorrhagic cholecystitis, such as that described by Ireneus,<sup>12</sup> are not considered to be similar to the cases reviewed and reported elsewhere in this paper.

Hemorrhage into the gastrointestinal tract, as indicated by routine stool examination, is of importance in cases of cholelithiasis. In a number of patients in whom anemia is apparently the primary disease, little attention is directed to the biliary system. It has long been well known, if not fully appreciated, that a considerable percent-

age of patients with cholelithiasis have no marked abdominal symptoms or signs. A considerable number of them have blood in the stools, a point that is frequently neglected in the differential diagnosis. In reviewing our own cases, it was found that in 13 per cent of 100 consecutive cases of cholelithiasis brought to operation there was blood in varying amounts in the stools. In some of the cases there was concomitant disease, which may or may not have been the cause of melena. For instance, a patient had had a duodenal ulcer excised twenty-four years previous to admission for cholelithiasis. At the earlier admission, however, there was no blood in the stools. Another patient had diverticulosis of the colon, which may or may not have accounted for the presence of blood. Other disease, such as carcinoma of the breast, may be discounted as noncontributory to the finding of blood in the stools. In cholecystitis without cholelithiasis, 8 per cent of the cases with this finding in a series of 100 consecutive cases have been operated on at the Beverly Hospital in recent years.

## CASE REPORTS

CASE 1 S S (No 54359), a 57-year-old, Jewish housewife, had had several previous hospital entries. Twenty-two years prior to admission she had a resection of the left ovary, left salpingectomy, right salpingo-oophorectomy, ventral fixation of the uterus, perineorrhaphy and dilatation and curettage. Fifteen years after the initial operation, she had a second perineorrhaphy and also an anterior colporrhaphy. Up to eight months prior to this admission the patient was in good general physical condition except for a 7-year history of occasional attacks of asthma. A careful history taking, however, revealed that as long as 1 year prior to admission she had had a sense of fullness in the epigastrium after eating. This usually occurred directly after taking a meal and was never accompanied by actual abdominal pain, although there was considerable gaseous distention. Some relief was obtained from the ingestion of sodium bicarbonate. There was no history of nausea, vomiting, jaundice, dark urine or tarry, bloody or clay-colored stools.

Eight months before the patient entered the hospital, she developed pain radiating from the substernal region to the back, especially on the left side, and extending into the arms. At that time a diagnosis of coronary disease was made and treatment was given accordingly. Shortly thereafter, because of an idiopathic anemia, the patient was given iron and liver therapy and placed on a special diet. One month later she began to have tarry or black stools. This may have been due to the oral administration of iron, because during 1 week of abstinence from iron the stools became brown. Four months later, during a stay at this hospital for bronchial asthma, hypertrophic arthritis, secondary anemia, possible gall-bladder disease and coronary insufficiency with healed myocardial infarct, the stools revealed a +++ test for occult blood, the reason for which was not immediately explained. A moderate secondary anemia with a hematocrit of 30 per cent quickly resulted. Extensive x-ray study of the gastrointestinal tract and gall bladder revealed no gastrointestinal cause for the melena, but the gall bladder was seen to be diseased. An attempt by an internist to determine the cause of secondary anemia following discharge also failed. Tenderness in the right upper quadrant of the abdomen,

\*From the Department of Surgery, Beverly Hospital.

†Resident in surgery, Beverly Hospital.

‡Chief surgeon, Beverly Hospital.

unexplained melena and secondary anemia continued, the anemia progressing until the red-cell count was 2,000,000 and the hemoglobin 40 per cent. There were four admissions for transfusion only during the 2 months prior to the final admission. This procedure was necessary because the patient persistently refused an exploratory laparotomy that the surgical staff advised on the basis of x-ray evidence of gall-bladder disease, together with bleeding from the gastrointestinal tract.

Physical examination on admission revealed a well developed, somewhat obese, moderately ill, woman complaining of pain in the right upper quadrant of the abdomen. She was not cyanosed, dyspneic or jaundiced. The temperature was 101°F, the pulse 92, the respirations 22, and the blood pressure 140/80. The abdomen was slightly obese but not distended and contained a well healed scar low in the midline. The liver edge was palpable 3 fingerbreadths below the costal border at the right midclavicular line. Just below the liver edge there was felt a dome-shaped mass 2 cm in diameter that was exquisitely tender. The mass was freely movable but seemed to move synchronously with the liver on deep breathing. The kidneys were not palpable, nor was the spleen. No other masses were felt. No hernia was demonstrable. There was no appreciable rebound tenderness or muscle spasm.

The urine was essentially normal except for the presence of sugar. The hemoglobin was 55 per cent, the red-cell count 2,610,000, and the white-cell count 6350, with 77 per cent neutrophils, 21 per cent lymphocytes and 2 per cent monocytes. The reticulocyte count was 1.1. A blood smear was not remarkable. The total protein was 7.4 gm per 100 cc. The albumin-globulin ratio was 1.4. The blood nonprotein nitrogen was 34 mg per 100 cc, and the blood-sugar level 140 mg. The patient at that time was taking 40 units of regular insulin daily. The blood Hinton reaction was doubtful. The hematocrit was 32 per cent.

X-ray examination of the gastrointestinal tract was negative. Examination of the gall bladder after the administration of dye led to a diagnosis of pathologic gall bladder.

During the hospital stay the patient was transfused several times, beginning immediately after admission. On the 3rd hospital day, with a preoperative diagnosis of an abdominal mass in the right upper quadrant, of undetermined source and nature but probably malignant, mild, uncomplicated diabetes mellitus and unexplained melena, a laparotomy was performed through an incision in the right upper rectus muscle. The gall bladder was distended and filled with stones and large blood clots. The liver was enlarged but was otherwise not remarkable. Cholecystectomy and biopsy of the liver were carried out. The common duct was not explored. The patient was transfused after operation. Postoperatively the temperature spiked to 101.5°F on several days, but otherwise improvement was steady. The drain was removed on the 8th postoperative day, following which the temperature rose and a small wound abscess developed, a culture of which grew *Staphylococcus aureus*. Following this mild complication, recovery was uneventful. The diabetes was controlled fairly well with insulin and diet. The stools showed no further blood. The pathological report revealed chronic cholecystitis with cholelithiasis and a malignant hemangioendothelial sarcoma. Apparently this lesion had been removed in toto. There was no evidence of metastasis at operation and there has been no recurrence of symptoms, or anemia.

**Comment** This case at first seems to support the belief that bleeding from the gall bladder is prone to occur in patients with vascular disease. The patient was diabetic, and although she had no marked external arteriosclerosis, there was a history of coronary insufficiency and she was at an age when diabetic arteriosclerosis begins to manifest itself. The presence of the hemangioendothelial sarcoma within the gall bladder, however, may well have accounted for the bleeding. This finding actually seems to exclude this case from the group of true hematocholecyts to which the other 3 cases presented here clearly belong.

**CASE 2** D W (No 26893), a 30-year-old housewife, was admitted 9 years after an initial attack of severe epigastric pain. Other attacks subsequently occurred, and in all of them the pain was constant and acute in onset. A similar attack 6 months prior to admission had lasted for only 1 hour.

The present attack centered in the right upper quadrant of the abdomen, and the patient ascribed her symptoms to ice cream that she had eaten a few hours previously. She had vomited bile-colored fluid many times. She had never been jaundiced and had noticed no tarry or clay-colored stools or dark urine. She had passed no gross blood with stools.

Physical examination revealed an obese woman with acute distress in the upper abdomen. The temperature was 98.2°F, the pulse 76, and the respirations 20, and the blood pressure 120/80. The abdomen was obese but soft. There was marked tenderness in the right upper quadrant and throughout the entire epigastrium. There was no rebound tenderness, no palpable mass, and no hernia or other pathologic findings. Peristalsis was normal.

The urine was essentially normal. The hemoglobin was 97 per cent, the red-cell count 4,940,000, and the white-cell count 16,900 with 79 per cent neutrophils, 18 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. The stool was brown and contained no blood. The icterus index was 8.2. The van den Bergh reaction was indirect. The bilirubin was less than 2 mg per 100 cc. A blood Hinton test was negative. In a test for urinary diastase, 32 cc. of starch solution was digested by 1 cc. of urine. The blood nonprotein nitrogen was 26 mg per 100 cc., and the blood sugar 80 mg.

Three days after admission, x-ray examination of the gall bladder following intravenous administration of dye revealed no concentration of dye. No stones were visible. An x-ray diagnosis of pathologic gall bladder was made.

On the 5th hospital day, with a preoperative diagnosis of acute cholecystitis and cholelithiasis, a laparotomy was performed under spinal anesthesia through an incision in the right upper rectus muscle. The gall bladder was moderately distended, and the mesentery was adherent to it. On aspiration of the gall bladder a large amount of fresh gross blood was obtained. There were several faceted stones and two ulcerations in the mucosa. No exploration of the common duct was carried out. The pathological diagnosis was the subsiding phase of a chronic recurrent cholecystitis and cholelithiasis, with formation of small ulcers. The postoperative course was uneventful, and the patient was discharged on the 15th postoperative day.

**Comment** This case is probably typical of the cases of cholecystitis with cholelithiasis in which there is unexplained hemorrhage into the gall bladder. There was no blood dyscrasia and no known vascular disease, but microscopic sections of the extirpated gall bladder revealed marked sclerotic changes in the blood vessels.

**CASE 3** H R (No E-4154), a 68-year-old housewife, was admitted with a chief complaint of acute epigastric pain radiating to the back. Pain had begun on the previous day. The patient had had "gall-bladder trouble" during the 24 years prior to admission. The attacks, which lasted for 10 to 15 minutes and occurred several times yearly, consisted of discomfort in the midepigastrium, with radiation of dull pain to the right costal margin and beneath the right shoulder blade. There was also a sensation of gaseous distention. Between attacks there was a slight degree of indigestion, characterized by gaseous distention following meals. The patient generally refrained from fatty foods but found that she could occasionally take fat in small amounts. There was no history of jaundice, dark urine or clay-colored or tarry stools prior to the most recent attack. There had never been chills.

Twelve years prior to admission the patient was seen at a diagnostic clinic, where she was told that she had "gall-bladder trouble." She was not operated on, since it was thought desirable to reduce the body weight, which was well over 200 pounds, before surgery was attempted. Six weeks before admission, she had an unusually severe attack, accompanied for the first time by mild nausea and vomiting. X-ray films taken elsewhere revealed impaired function of the gall bladder. There was no jaundice with the present attack, but the urine was mahogany-colored. The bowel movements had been scanty and clay-colored for the last few days. There was no history of diarrhea, blood in the stools or tarry stools.

Physical examination on admission revealed an obese

woman in moderate epigastric distress. There was a slight icteric tinge to the skin and scleras. The temperature was 98°F, the pulse 100, the respirations 20, and the blood pressure 186/104. The abdomen was soft and nontender. No masses were palpable in any quadrant, nor was there muscle spasm.

In a test for urinary diastase 4 cc of starch solution was digested by 1 cc of urine. The blood nonprotein nitrogen was 28 mg per 100 cc and the blood sugar 87 mg. The icterus index was 17. The van den Bergh reaction was immediate and indirect. The bilirubin was 2.89 mg. A blood Hinton test was negative. The prothrombin time was 35 seconds (normal, 17 seconds). The blood amylase was 45 mg per 100 cc. The stool revealed a +++ test for blood, and the vomitus a +++ test. The urine gave a ++ test for bile, the sediment contained a few red and white cells and bacteria. The hemoglobin was 71 per cent, the red-cell count 3,740,000, and the white-cell count 8400, with 68 per cent neutrophils, 30 per cent lymphocytes and 2 per cent monocytes. A blood smear was not remarkable.

The electrocardiogram was negative except for mild left-axis deviation, which was ascribed to left ventricular hypertrophy.

During the hospital stay there were recurrent attacks of nausea, vomiting and upper abdominal pain. Most of the stools contained blood. The bile disappeared from the urine 9 days after admission.

A preoperative diagnosis of chronic cholecystitis, cholelithiasis, choledocholithiasis and hemorrhage from the gall bladder was made. Under spinal anesthesia, a laparotomy was performed through an incision in the right upper rectus muscle, and an adherent gall bladder containing large clots of gross blood and numerous stones was removed. There were two ulcerations in its mucosa. The common duct contained three stones. The pancreas was normal. No other disease was found in the right upper quadrant of the abdomen. A T-tube was placed in the common duct, and a large amount of bile drained postoperatively. The postoperative course was uneventful, and the patient was discharged on the 23rd postoperative day. The pathological diagnosis was chronic and acute cholecystitis, cholelithiasis and blood clot in the gall bladder. There was no evidence of malignancy.

**Comment.** This case was remarkable in that extensive studies were undertaken to determine the exact cause of bloody stools that coexisted with known cholelithiasis and cholecystitis. By a process of exclusion, the only feasible explanation for the presence of blood in the stools was bleeding from the gall bladder, so that this diagnosis was made preoperatively. Such a diagnosis is highly unusual in the medical literature on this subject.

This patient suffered from hypertensive and arteriosclerotic heart disease of a mild sort, and it is known that bleeding from the gall bladder is likely to occur in patients with arterial and venous disease. Heusser<sup>1</sup> points out that the real reason for hemorrhage from the gall bladder is probably intrinsic pathologic changes in blood vessels rather than direct or mechanical erosion of the vessels by stones. Microscopic studies of this case seemed to confirm this theory.

**CASE 4.** W. C. (No. J-4033), a 44-year-old man was admitted with a history of attacks of sharp pain in the right side of the chest, accompanied by nausea and four spells of vomiting, of 5 days' duration. The vomitus consisted of undigested particles of food. Following the pain in the chest there was dull pain in the right upper quadrant of the abdomen, which persisted and became worse shortly before admission. During the 48 hours prior to admission, the nausea and vomiting subsided. The patient had been treated, for 3 days by his local physician, the treatment consisting of bed rest and nothing by mouth except whisky and water. The patient had never been jaundiced and had never noticed clay-colored, tarry or bloody stools. His past history revealed nothing remarkable except constipation during the week prior to admission. There had been no previous surgical operations or hospitalizations.

Physical examination on admission revealed a stocky, well developed and well nourished middle-aged man in mild upper abdominal distress. He was alert and co-operative and was not cyanotic, dyspneic or jaundiced. The temperature was 99°F, the pulse 88, the respirations 20, and the blood pressure 152/82. The heart was enlarged to the left

and downward. The apex impulse was felt in the 6th intercostal space outside the midclavicular line. The heart sounds were of good quality, and the rate was regular. There were no thrills or murmurs. The abdomen was obese. There was exquisite tenderness around the region of the gall bladder in the right upper quadrant, where a large mass, assumed to be a distended gall bladder, was readily palpated. The spleen and kidneys were not felt. There was no evidence of hernia. Peristalsis was normal. The rest of the abdomen was soft and nontender. There was no demonstrable fluid. An admission diagnosis of subsiding acute cholecystitis and cholelithiasis was made.

The urinalysis was negative except for the presence of 30 to 40 white cells per high-power field in the sediment. The red-cell count was 5,030,000 and the hemoglobin 97 per cent. The white-cell count was 10,350, with 79 per cent neutrophils, 16 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils. A blood smear was not remarkable. Examination of the stool revealed mucus but no blood. A blood Hinton test was negative. The nonprotein nitrogen was 28 mg per 100 cc, the blood sugar 77 and the vitamin C level 0.35 mg. The total protein was 5.9 gm per 100 cc, the fibrinogen being 0.7 gm, globulin 2.1 gm and the albumin 3.1 gm, an albumin-globulin ratio of 1.5.

X-ray examination confirmed the presence of gallstones, and on the 3rd hospital day, under spinal anesthesia, the abdomen was opened through an incision in the right upper rectus muscle. The gall bladder was found to be greatly distended, and stones were palpated in it. There were no ulcerations in the serosa. Cholecystectomy was carried out without undue difficulty, and the patient had an uneventful postoperative recovery until the 4th postoperative day, when the lower end of the rectus incision opened and there was a slight evisceration of omentum through the wound. Resuturing was immediately carried out under spinal anesthesia. Following this, no further complications developed, and the temperature did not rise above 99.6°F after the second operation.

When the gall bladder was opened following operation, it was found to contain several clots and a massive hemorrhage. There were also present the pathologic changes suggestive of chronic and acute cholecystitis, as well as gallstones. A pathological diagnosis of bleeding gall bladder revealing a marked chronic and acute inflammatory process was made. The microscopic examination of sections from the gall bladder revealed the mucosa to be swollen and edematous and the blood vessels to be markedly dilated. The sclerotic changes in the vessels described in Cases 2 and 3 were present but not marked.

## SUMMARY

The literature on hemorrhage of the gall bladder is briefly reviewed, and 3 cases of idiopathic hemorrhage are reported. A case of hemorrhage from hemangioendothelial sarcoma of the gall bladder is also described.

It seems quite likely, after reviewing our operative cases and those collected from other workers, that sclerotic changes in the vessels of the gall bladder are the underlying cause of such hemorrhage. Mechanical irritation from stones seems to be a secondary consideration.

The only lesson to be learned from these case studies is that more attention should be directed to the finding of blood in the stools of patients in whom cholelithiasis has not been excluded. It is probable that many cases of unexplained secondary anemia or of blood in the stools are due to cholelithiasis.

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## CLINICAL NOTE

### SENSITIVITY TO TINCTURE OF MERTHIOLATE

CAPTAIN LESTER LIPSON, M C, A U S

**T**INCTURE of Merthiolate is widely used as a skin antiseptic and a preoperative preparation. This tincture is a 1000 alcohol acetone aqueous solution of sodium ethyl mercurithiosalicylate. Sensitivity to it is rare, but because this may occur and cause a disabling dermatologic complication, the present report seems justified.

#### CASE REPORT

A 21-year-old soldier was admitted to the 101st General Hospital on April 14, 1945. Three weeks previously, he had fallen from a vehicle suffering abrasions of both knees. After 5 days of self-treatment by dressing the abrasions with his first-aid packet, without noticeable improvement, the patient reported to the dispensary, where the abrasions were painted with Tincture of Merthiolate. This treatment was repeated daily for 5 days, by which time the skin had blistered, so that the treatment was stopped. The skin lesions, however, became more disabling during the next few days, and the patient was sent to this hospital. As a civilian he had had numerous attacks of poison-ivy dermatitis.

At physical examination the patient did not appear to be seriously ill. The extensor surfaces of both knees and the adjacent thigh and leg areas were the sites of a secondary infected dermatitis. There were many blebs and bullae, filled with serous or purulent fluid, and inflammatory erythema and induration were present throughout the area of involvement.

Patch tests were done in the usual manner on the flexor surfaces of the forearm with the following substances: Tincture of Merthiolate, aqueous Merthiolate solution, alcohol, acetone, Tincture of Metaphen (4-nitro-anhydro-hydroxy-mercury-ortho cresol), aqueous solution of Mercurochrome (dibrom-oxymercuri-fluorescein-sodium), and mercurial ointment (30 per cent metallic mercury). In the test with Tincture of Merthiolate, the patch had to be removed in 12 hours because of severe pruritus. The reaction exactly mimicked the lesions on the knees, showing blebs, vesicles and induration, and it spread to involve an area five times the size of the patch. Two weeks later, evidence of the reaction still remained (Fig 1). A reaction of equal severity resulted from

the test with the aqueous solution of Merthiolate. All the other patch tests were negative after 48 hours.

The lesions were treated as those of a pyoderma and cleared up without difficulty. Considerable discoloration persisted.

The material used for the patch test, which was performed in England, was not the same as that originally applied to the knees. The mercurials other than Merthiolate elicited no reaction and the tests with acetone and alcohol were similarly negative. All the tests were applied to areas not pre-

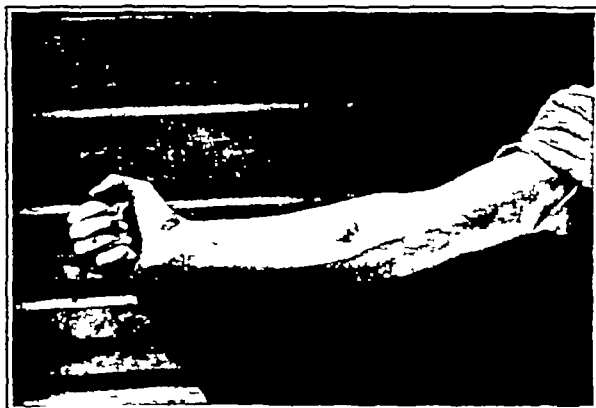


FIGURE 1 Photograph of the Reaction  
This photograph was taken two weeks after the patch test with Tincture of Merthiolate had been applied.

viously treated by any other drug. One must conclude that the sensitivity was due specifically to Merthiolate, since there were positive reactions both to the tincture and to the aqueous solution.

#### SUMMARY

An unusual case of skin sensitivity to Merthiolate is presented. No sensitivity to other mercurials could be demonstrated. Because of the widespread use of this skin antiseptic, the possibility of such sensitivity should be kept in mind.

## MEDICAL PROGRESS

## DIABETES MELLITUS

ELLIOTT P JOSLIN, M D \*

BOSTON

THIS review of progress in diabetes mellitus will consider advances in knowledge concerning alloxan and carbohydrate metabolism, recent papers on diabetic neuropathy, two articles dealing respectively with diabetes in children and with facts concerning the disease in Finland and, finally, associations, societies, foundations and trusts primarily interested in the problems brought about by this disease

## ALLOXAN

Duff,<sup>1</sup> a well informed scientific investigator whose opinion is greatly respected and whose review of the pathology of the pancreas in experimental diabetes mellitus is most complete, makes the following statement "It is most improbable at present that alloxan plays a role in the etiology of human diabetes" Despite this assertion, I cannot escape the clinical conviction that the discovery of the specific action of this substance in destroying the beta cells of the islands of Langerhans has brought medical scientists nearer to the explanation of diabetes than has any step made hitherto — including partial pancreatectomy and the injection of anterior-pituitary extract Since the progress reports of 1944 and 1945 in this journal,<sup>2, 3</sup> distinct advances have been made in the knowledge of alloxan that strengthen this belief More and more the specificity of its action in animals and birds has been confirmed Although in the human body alloxan has not been demonstrated in metabolic processes, particularly that of uric acid, from which it can be derived, tests for it have identified its presence in the tissues of animals

The first of these tests was devised by Leech and Bailey<sup>4</sup> It detects alloxan in quantities as small as 0.05 mg in blood, and with slight modifications in certain tissues, including the pancreas It has been found that alloxan reaches its highest level at the end of injection, following which it rapidly decreases, with complete disappearance from the blood in five minutes It is found in the tissues of the pancreas in quantities of 24 to 56 mg per 100 gm at the end of the injection

A second test, devised by Banerjee, Dittmer and du Vigneaud,<sup>5</sup> involves the conversion of alloxan into riboflavin, a phenomenon that is measured by microbiologic and fluorometric techniques It is useful only for the detection of alloxan in aqueous solu-

tions These authors confirmed the results of Leech and Bailey regarding the stability of alloxan at various hydrogen-ion concentrations They showed that alloxantin, which acts similarly to alloxan, yields the same amount of riboflavin as does alloxan Incidentally, the fact that alloxan and alloxantin are closely akin to a vitamin is interesting, even if not yet proved to be significant Moreover, if alloxan can be converted into riboflavin, the reverse may well be possible

Ruben and Tipson,<sup>6</sup> in a preliminary paper, have recently reported the detection by another method of what they assumed to be alloxan in the normal livers of the steer, cat, calf, domestic fowl, guinea pig, lamb, rabbit and rat

Finally, Archibald<sup>7</sup> has described six methods for the detection of alloxan under varying conditions As a result of his tests, he concludes that the blood plasma and urine of normal human beings and dogs must contain less than 0.02 mg of alloxan per 100 cc The addition of alloxan to filtrates of whole blood containing glutathione results in the formation of dialuric acid Archibald states that the possibility that circulating blood normally contains small amounts of alloxan should not be overlooked

These various tests for alloxan and the demonstration of its existence and reactions under varying conditions in animals count toward its conceivable importance in diabetes

Substances closely akin to alloxan act similarly to it The first of these is alloxantin, which was referred to in my last progress report<sup>3</sup> Styryl quinoline No 90, which was originally found by Dunn to destroy the islet cells, has not as yet been proved to cause diabetes, but Bruchmann and Wertheimer<sup>8</sup> have shown that methylalloxan, dimethylalloxantin, dialuric acid and methyl dialuric acid produce it in rats when injected intravenously The demonstration that these bodies, so closely related to alloxan, also cause diabetes suggests that if the search is continued, the actual chemical that plays the diabetogenic role can be found

Neutralized alloxan or alloxan dissolved in either rabbit or human blood plasma is not diabetogenic This discovery, of which I was aware a year ago, has now been published by Leech and Bailey<sup>4</sup> Weinglass, Frame and Williams<sup>9</sup> have gone a step farther and shown that 3-4, diamino-toluene, orthophenylene-diamine or sodium bisulfite, if injected intravenously within five minutes before alloxan is given,

\*Clinical professor of medicine, emeritus, Harvard Medical School medical director, George F Baker Clinic, New England Deaconess Hospital

prevents its diabetogenic action. A marked decrease in the blood glutathione invariably follows the injection of a diabetogenic dose of alloxan.<sup>10</sup> When the molecular equivalent (400 mg per kilogram of body weight) of reduced glutathione is injected immediately before and during the injection of 200 mg of alloxan per kilogram of body weight, the glutathione fails to prevent the subsequent diabetes. The blood-alloxan and blood-reduced-glutathione determinations made in 6 rabbits injected with 200 mg per kilogram suggest that there is an immediate reaction between alloxan and blood-reduced glutathione, with a tendency toward the complete disappearance of both. The critical level at which blood-reduced glutathione changes tend to parallel the development of diabetes is about 100 mg per kilogram. During the slow development of diabetes through repeated small doses of alloxan, the blood-reduced glutathione tends to be increased over normal, with a sudden drop to normal as diabetes ensues.<sup>4</sup>

The rapidity of the action of alloxan in causing destruction of the islets of Langerhans and producing diabetes is so unlike the speed of development of the disease in human beings that the demonstration by Bailey, Bailey and Leech<sup>10</sup> that repeated doses over a long period also bring on the disease naturally appeals to a clinician. This rapid destruction of the islets by a single large dose of alloxan, however, was shown by Goldner<sup>11</sup> and Gomori and Goldner<sup>12</sup> when they temporarily ligated the blood supply to half the pancreas and injected alloxan. The temporary ligatures were released five minutes later, and histologic sections revealed the absence of changes in the islet cells in the part of the pancreas deprived of blood for this period of time, whereas in the remaining portion the usual necrosis of the islets was present.

Marked differences exist between alloxan diabetes and the diabetes caused by partial pancreatectomy and the injection of anterior-pituitary extract. In the former particularly, the disease can be prevented or even cured if hyperglycemia is avoided, this is distinctly not the case with alloxan diabetes. Differences in the pathologic picture have been emphasized by Duff<sup>1</sup> as follows:

The hydropic degeneration of the beta cells produced by partial pancreatectomy appears to be identical with that produced by anterior-pituitary extracts. This change is at first reversible and only later progresses to irreversible cell damage. In both instances hydropic degeneration is probably caused by the excessive functional demands associated with hyperglycemia. In alloxan diabetes, the beta cells of the islets show, from the beginning, degenerative changes that lead quickly to necrosis without the appearance of a stage in any way resembling hydropic degeneration. The necrosis is probably caused by the direct action of alloxan on the islet cells, and this injury is irreversible.

It should not be overlooked, however, that there are resemblances between alloxan diabetes and the

diabetes caused by partial pancreatectomy and anterior-pituitary extract. Thus, Bailey, Bailey and Leech<sup>10</sup> found that in the diabetes produced in one to three weeks by the daily injection of small doses of alloxan (40 mg per kilogram of body weight), the pancreas underwent a series of changes quite different from those following a single massive injection. With the small doses a wide variety of changes in the beta cells was apparent. Some of them looked almost normal, whereas in others degeneration was the only evidence of injury, and still others showed hydropic degeneration. On the other hand, these authors also state, "This complex picture of normal cells, slightly injured cells, cells with hydropic degeneration, irreversibly damaged cells and a mitosis in a single islet is not clearly duplicated in any other form of experimental diabetes or in human patients," but I have always understood this statement to mean that in these animals a remarkably comprehensive picture in a single islet can be found for which one would need to search in several islets in the human being.

Hughes and Hughes<sup>13</sup> injected rats subcutaneously with repeated small injections of alloxan. They found that the larger and presumably older beta cells of the pancreas succumbed to the toxic action of concentrations of alloxan that were too low to damage young beta cells.

Further studies on animals with slowly produced alloxan diabetes must be made and reported before one can reach a final conclusion that the histologic picture of alloxan diabetes is essentially different from that of the other two experimental forms of the disease. Kennedy and Lukens,<sup>14</sup> as well as Bailey, Bailey and Leech,<sup>10</sup> also noted hydropic degeneration in an animal with alloxan diabetes, but they attributed it to the effect of hyperglycemia on beta cells that had escaped destruction by the alloxan.

In this connection, the experience of Carrasco, described in my last report,<sup>3</sup> is of interest. A dog that he injected with alloxan developed diabetes in a mild form but subsequently recovered. This result makes it clear that the pancreas of an alloxan-injected animal may regenerate just as does the pancreas in diabetes induced surgically or by anterior-pituitary extract. Furthermore, it should be borne in mind that in diabetes in human beings, hydropic degeneration has steadily grown rarer and rarer, with an accompanying decrease in the mortality from the disease in the first days, weeks and months following its onset. It is true that further experiments with alloxan are needed before it can be determined whether the fibrosis and hyalinization of the islands, so frequent in human diabetes, will appear when experimental conditions are set to allow an opportunity for it. Moreover, too little time has been spent by investigators of alloxan diabetes in studying the possibility of altering its course by diet, reduction of blood sugar and the



giving of insulin. Thus, Burn, Lewis and Kelsey<sup>15</sup> demonstrated that rats with alloxan diabetes when placed on a high-fat diet showed a disappearance of the glycosuria, which remained absent until the normal diet had been resumed. An abrupt resumption of the high-fat diet was accompanied by some ketonuria, but on a gradual increase of the fat component the glycosuria disappeared without the development of ketonuria. In other words, alloxan diabetes in rats may at times be controlled by diet. After successive periods of a high-fat diet, the glycosuria seen on a return to a normal diet steadily diminished.

The regular appearance of diabetic cataracts in rabbits, and less frequently in rats, observed by Bailey, Bailey and Leech within two months after injections of alloxan, reminds one of the frequency of such a complication in human beings with diabetes. Such cataracts have been shown in partially depancreatized dogs and also in depancreatized rats,<sup>16</sup> and I understand have been reported in the pituitary diabetes of a dog. The observations of the Boston group have been confirmed by Chesler and Tislowitz<sup>17</sup> in rats, and personal communications state that cataracts have been found at various other laboratories, in Cleveland and Philadelphia.

Various birds, such as owls, ducks and chickens, have been intravenously injected with alloxan by Scott, Harris and Chen<sup>18</sup> without developing diabetes. Pigeons, however, developed hyperglycemia and showed normal islets, but with occasional hydropic degeneration. Pigeons, like human beings, do not convert uric acid into allantoin, but they respond to alloxan in the same way as do animals that produce allantoin from uric acid. The same holds true for the Dalmatian hound. Goldner<sup>11</sup> noted the occurrence of a whitish deposit, identified as sodium urate, in the pericardium, pleura and liver of many diabetic pigeons with diabetes. This was not observed by Mirsky<sup>19</sup> in his report of experiments with alloxan in ducks. Hyperglycemia was produced, but as in pigeons, there was only partial necrosis of the islands of Langerhans. Mirsky found necrosis without diabetes when 50 to 750 mg of alloxan per kilogram of body weight was injected into the wing vein of ducks. Two hundred milligrams caused death within three to forty-eight hours. Hyperglycemia occurred in some birds but not in others. Hypoglycemia was not noted. The islets of ducks appear to be sensitive to large doses of alloxan, but Mirsky states that these birds do not require intact islands to maintain carbohydrate metabolism and thus differ markedly from other species. One duck, following the injection of 50 mg of alloxan per kilogram, showed necrosis in nine days but no hyperglycemia.

Ramos<sup>20</sup> reports hyperglycemia with sugar values reaching 242 mg per 100 cc in turtles two days after the injection of alloxan. Goldner and Gomori<sup>21</sup> pur-

sued their studies on carbohydrate in uric acid metabolism in pigeons following injections of alloxan. The blood sugar was increased from the normal daily level of 150 mg to 300 to 400 mg. Smaller doses caused a similar syndrome but without a rise in the blood sugar. The uric acid increased from the pre-*alloxan* level of 4.2 to 7.0 mg to 8 to 34 mg in six hours and from 9 to 135 mg in twenty-four hours. Such an increase has been clinically recognized in human beings as a symptom of visceral gout. It was accompanied by a conspicuous atrophy of the musculature.

The more one experiments with alloxan, the more bizarre are the results. Thus, Thorogood and Zimmermann<sup>22</sup> found that dogs made diabetic with alloxan and subsequently depancreatized required only one third of the insulin needed prior to pancreatectomy. Direct ligation caused little or no drop in the need for insulin. They also found that depancreatized dogs developed acidosis much more easily than did those with alloxan diabetes, although the diabetes in the latter was apparently severer. They thought that there might be a second hormone, possibly residing in the alpha cells, that acted in opposition to insulin and tended to prevent acidosis and coma.

Monkeys develop diabetes and also acidosis following injections of alloxan. This is unusual, as is pointed out by Goldner and Gomori,<sup>21</sup> because monkeys do not always develop severe diabetes following pancreatectomy. According to Orias,<sup>23</sup> rats with 95 per cent of the pancreas removed are more resistant to the diabetic action of alloxan than are normal controls, but with repeated subliminal doses at ten-day intervals they tend to develop diabetes more readily than do normal rats.

Alloxan when introduced into the alimentary tract of rats causes the same changes in the islets of the pancreas, according to Ruben and Yardumian,<sup>24</sup> as those that it produces when injected into the tissues or peritoneal cavity. When this method is employed with a dosage sufficient to produce diabetes, however, distinct hepatic and renal damage occur.

Assays of the pancreases of dogs with alloxan diabetes for insulin show about 0.5 unit per gram, in contrast to the pancreases of normal dogs, which contain 2 or 3 units per gram.<sup>25</sup> For a comprehensive report of the factors affecting the insulin content of the pancreas, one should consult Haist's article.

The hyperglycemia that early results in animals injected with alloxan has been ascribed to gluconeogenesis in the liver. It has been duplicated by the simultaneous injection of adrenalin and insulin into animals. It has been prevented by the injection of alloxan into functionally or anatomically adrenalectomized rabbits, according to Goldner and Gomori.<sup>26</sup> Houssay, Orias and Sara<sup>27</sup> found that hyperglycemia did not occur in hepatectomized dogs or toads. They observed it in adrenalectomized

animals and dogs with a previous section of the splanchnic nerves and in recently hypophysectomized toads

The hypoglycemia that follows hyperglycemia in animals with alloxan diabetes is not directly caused by alloxan, because it does not occur in depancreatized dogs or dogs already made diabetic with alloxan. Furthermore, the injection of alloxan into eviscerated cats is not followed by a reduction in blood sugar.<sup>25</sup> Hypoglycemia has been thought to be due to the liberation of alloxan from the necrosing degenerated beta cells, and Goldner and Gomori<sup>26</sup> state that whenever hypoglycemia develops, diabetes follows if the animal survives. From this conclusion Houssay et al dissent. In fact, their conclusions regarding the triphasic blood-sugar changes in animals with alloxan diabetes are as follows:

(1) The liver is essential for the initial hyperglycemia produced by alloxan. Hyperglycemia is observed in adrenalectomized animals and those with section of the splanchnic nerves. It must be attributed principally to a direct action of alloxan on the liver. (2) The secondary hypoglycemia is not due to liberation of insulin, but to an extrapancreatic effect, probably lack of glucose production by the liver. The liver of the animal already in a diabetic condition is generally insensible to this action of alloxan. (3) The final hyperglycemia is mainly due to the destruction of the beta cells of the islets of Langerhans, and becomes permanent if the animal survives. (4) The liver plays an important role during the three phases of modification of blood sugar level.

Kirschbaum, Wells and Molander<sup>29</sup> conclude as follows from their experiments:

An initial hyperglycemia did not appear in either adrenalectomized or hypophysectomized rats injected with alloxan. With the doses of alloxan used, hypoglycemic convulsions did not appear in any of 15 intact animals, whereas convulsions occurred within six hours in all of 14 adrenalectomized and in 9 of 10 hypophysectomized animals. In the absence of the adrenal medulla the reaction to alloxan was the same as in intact animals. Removal of the adrenal cortex (regenerated cortex following adrenal enucleation) resulted in the same reaction as total adrenalectomy.

Foglia, Oras and Sara<sup>30</sup> injected alloxan subcutaneously into rats and found a prolonged initial hyperglycemia lasting for three to five hours, which was followed by a marked hypoglycemia. In previously pancreatectomized rats, however, subsequent injection of alloxan failed to affect the blood-sugar level.

Thomas and Emerson<sup>31</sup> showed that the pituitary glands of rabbits given intravenously 200 to 300 mg of alloxan per kilogram of body weight revealed degeneration of the basophils and in some cases areas of necrosis in the adrenal cortex. Rats receiving 400 mg per kilogram subcutaneously developed similar lesions. Janes and Friedgood<sup>32</sup> demonstrated that rats made diabetic with alloxan showed marked reduction or disappearance of their diabetic symptoms following adrenalectomy. Thus, they respond to adrenalectomy in a manner similar to that shown by pancreatectomized animals.

Pregnant rats injected with alloxan developed diabetes, according to Friedgood and Miller.<sup>33</sup> The

alloxan passed through the placenta but did not cause diabetes in the offspring. No reason for this is given. Chesler and Tislowitz<sup>17</sup> found that alloxan dwarfed the growth of immature rats. Lowry and Hegsted,<sup>34</sup> using rats on a thiamin-deficient diet, demonstrated that rats made diabetic with alloxan develop thiamin deficiency at approximately the same rate as normal controls, or perhaps slightly less quickly. Furthermore, the response of the diabetic animals to thiamin therapy was more marked than that of the controls. Schneider, Lewis, Moses and McCullagh<sup>35</sup> report diabetic retinitis associated with reduction of the plasma protein in rabbits made diabetic with alloxan. They describe changes in the lens in 15 rabbits.

With the aid of deuterium, Stetten and Boxer<sup>36</sup> found that on a diet that was 60 per cent carbohydrate one fourth of the urinary glucose formed by rats with alloxan diabetes was synthesized *in vivo* and the other three fourths was derived from the dietary carbohydrate. The proportion of liver glycogen synthesized from fragments smaller than hexose was greater than had been found in normal rats. Synthesis from fatty acids decreased to 5 per cent of the normal rate. This failure of the diabetic animal to utilize glucose in the synthesis of fatty acids constitutes a major metabolic defect in this disease.

Comparative studies of the action of alloxan on the islet cells of the pancreas and the convoluted tubules of the kidney in the rabbit, the dog and man have been published by Brunschwig and Allen.<sup>37</sup>

Interest in alloxan diabetes continues unabated. Published work in 1945 emanated from at least twenty-five different laboratories in eight countries. With the cessation of the war, one may expect this year twice the number of reports published in 1945.

#### CARBOHYDRATE CHEMISTRY

Carbohydrate chemistry has made marked strides in the last few years. Perhaps one of the most spectacular discoveries has been the synthesis of glycogen *in vitro* by Cori.<sup>38</sup> Even more recent is the work of Hastings,<sup>39</sup> who has shown by the use of radioactive tracer elements that a substance seemingly as remote from carbohydrate as bicarbonate of soda can under suitable conditions take part in the creation of a carbohydrate molecule. The influence of insulin on blood pyruvate localized in a general way the action of insulin, but the crucial point in the breakdown of carbohydrate at which there is interference in its utilization, as in diabetes, has always been a mystery. Evidence that may furnish a valuable clue to the solution of the problem has recently been reported by Price, Cori and Colowick.<sup>40</sup> In the utilization of glucose by animal tissues this substance is ordinarily transformed to glycogen by oxidation, which is catalyzed by hexokinase (glucose and adenosine triphosphate glucose-6 phosphate and adenosine diphosphate). According to these au-

thors, anterior-pituitary extract inhibits this reaction, as shown either by injecting rats with it prior to the preparation of tissue extracts or by adding it to the enzyme preparation in vitro. Moreover, — and this is of vital importance, — this inhibition can be counteracted by insulin, either in vivo or in vitro.

Of particular interest is the statement of Price et al. that rats made diabetic by the injection of alloxan yield tissue extracts that show the same enzyme activity curve as do those obtained from rats made diabetic by anterior-pituitary extract. The brain, they point out, is an apparent exception, since brain extracts prepared from rats injected with alloxan or with anterior-pituitary extract do not show an inhibition of hexokinase activity. Brain extracts can, however, be inactivated by addition of anterior-pituitary extract in vitro.

Anterior-pituitary extract does not inhibit the conversion of glycogen to lactic acid in muscle extract. In a dialyzed liver dispersion, when oxygen consumption is measured, oxidation of glucose is inhibited by anterior-pituitary extract, whereas that of fructose-6-phosphate and of pyruvate is not. Insulin releases hexokinase from inhibition by anterior-pituitary extract in all cases. It does not by itself enhance hexokinase activity under these experimental conditions. Price et al. state

Within a certain range the release of inhibition is proportional to the amount of insulin added in vitro. That the in vivo action of insulin is of a similar nature is indicated by the fact that muscle extracts prepared from diabetic rats after the injection of insulin show normal hexokinase activity. When insulin is reduced by cysteine, it no longer exerts its antagonistic effect against anterior-pituitary extract inhibition of hexokinase activity.

The authors promise to discuss in later publications the implications of this important discovery.

#### DIABETIC NEUROPATHY

An outstanding summary of diabetic neuropathy, with the listing of 171 references, as well as a contribution to the subject, has recently been published by Rundles.<sup>41</sup> Like the reviews by Duff<sup>2</sup> and Haist,<sup>26</sup> elsewhere cited, this work is to be held up as an example for future authors. All these articles deserve detailed comment, but the greater clinical importance of Rundles's paper forces me to give it preference.

Diabetic neuropathy has been described for over fifty years, and such names as Marchal de Calvi, Bouchard, Pavy, Leyden, Charcot and others less familiar have been associated with it. In 1936, Jordan<sup>42</sup> published a comprehensive summary of the data on neuritis available at the George F. Baker Clinic at that time. Rundles's article has been excellently reported in an editorial in the *Journal of the American Medical Association*,<sup>43</sup> to which those who do not have access to the original paper may turn. Several points made by Rundles, based on his experience with 125 cases among some-

what more than 3000 new diabetic patients during a seven-year period, deserve emphasis. Of these he studied 35 personally. From his intensive survey of the literature and his own observations, he reached definite conclusions, which are most important for any physician treating a diabetic patient. He states: "Most diabetics who develop organic disease of the peripheral nerves have had antecedent periods usually of months or years' duration of grossly neglected or poorly managed treatment. There is strong evidence that the disordered metabolism of diabetes mellitus itself is the etiologic factor in this as well as other accompanying diabetic complications." Rundles cites 5 cases of his series in detail. The first of these patients had typical symptoms of neuritis in the fingers and feet, following careless treatment for diabetes. In addition, she had discoloration of the right great toe and a blistered leg, which she attributed to a burn. The toe became dark purple, and pus exuded from it. After four weeks of hospitalization with orthodox treatment of the diabetes by an 1800-calorie diet containing 150 gm. of carbohydrate and 80 gm. of protein, and 10 units of insulin three times a day, the infected toe healed, although there was no definite alteration in the neurologic status.

The second case was that of a boy twenty years old with diabetes of six years' duration. In addition to characteristic symptoms of neuritis in the lower extremities and a so-called "low abdominal bulge," due to a quart of residual urine in the bladder, the patient showed the customary elevated spinal-fluid total protein (69 mg. per 100 cc.), first emphasized by Root.<sup>44</sup> Six weeks after admission, cloudy vision developed. An ophthalmology consultant, finding macular edema, punctate and flame-shaped hemorrhages and extensive areas of exudate, diagnosed severe diabetic retinopathy. Six weeks later there had developed an extensive proliferating retinopathy with both fundi filled with new-formed, dilated and tortuous veins and capillaries, with even more extensive deep and superficial hemorrhages but no further visual impairment. With diabetic control, supplemented by vitamins, the patient was discharged after four months little improved, but was seen at intervals for another eighteen months. The diabetes remained well controlled. He gradually gained in weight and strength, and the retinal hemorrhages became less extensive. To all physicians interested in diabetes the report of the condition of the eyes is significant. The consultant found the retinopathy much improved, reporting only minimal pigmentary disturbance in the regions of former hemorrhage, slight wrinkling and fibrotic scarring in different areas, a few new-formed blood vessels and a rare rosette-shaped hemorrhage. Rundles describes this result as the most astounding recovery of a diabetic retinitis of this type and severity he has ever seen or heard of. Unfortunately, such an experience is unique. Most ophthalmolo-

gists agree that diabetic neuropathy is almost always progressive and that retinitis proliferans rarely, if ever, improves.

The limits of space forbid the citation of the many interesting observations recorded by Rundles, but it must be pointed out that more than one fourth of his patients were less than forty years of age, with 8 of them twenty or younger. There was no predilection for welfare patients as compared with those of average or superior means, but all the patients showed lax diabetic care. No case was seen in which diabetic neuropathy actually preceded the appearance of diabetes mellitus. Furthermore, Rundles states that none of these patients were among those regularly attending his diabetic clinic or under the adequate supervision of competent physicians with provision for enlightened dietary management and checkup visits. These findings confirm the observations of Joslin and Root<sup>45</sup> that the symptoms of diabetic neuropathy always start during a time of uncontrolled diabetes.

Muscular cramps and aching in various parts of the body were early symptoms, and muscular weakness, especially of the legs, was almost uniformly present, 4 of the patients being able to go upstairs at home only by crawling on their hands and knees. Numbness, tingling and paresthesias, and shooting pains, characteristically worse on exposure to cold and at night, making the touch of bedclothes unbearable and sleep impossible, were frequent complaints. The lower extremities were most severely affected. The peroneal nerve was more vulnerable than the tibial, and the ulnar more vulnerable than the radial or median. Occasionally symptoms appeared in the pudendal, femoral or intercostal nerve areas or in asymmetrical areas in the extremities. The Achilles tendon reflexes were absent in 81 per cent of the cases, and patellar reflexes in 56 per cent, and each was diminished in an additional number of cases. Rundles considers diminished or absent tendon reflexes to be the most reliable single sign of diabetic peripheral nerve disease.

Gastrointestinal dysfunction, with diabetic, often nocturnal, diarrhea, and genitourinary and sphincter disturbances, are discussed. Rundles calls special attention to disease of the peripheral autonomic nerves, which was evidenced by damage to the peripheral sympathetic nerves and revealed by sweating, loss of vasomotor and pilomotor control and dependent edema. His knowledge in this regard was gained from the 35 patients whom he studied personally. Among these there were 26 patients who had dependent edema of the lower extremities appearing during the course of the neuropathy, which Rundles ascribed to involvement of the vasomotor nerves. Orthostatic hypotension and orthostatic tachycardia were observed and are also discussed. The association of diabetic neuropathy and retinopathy is emphasized, together with the fact that they may appear in the absence of hyper-

tension, impaired renal function and albuminuria. Wagener, Dry and Wilder<sup>46</sup> pointed out that retinal disease and peripheral-nerve disease were frequently associated in diabetic patients, and that 25 per cent of a large group of patients with diabetic retinitis had diabetic neuritis in addition. Rundles found that the converse relation, also held in his patients with diabetic neuropathy, since 43 (34 per cent) of the 125 patients had retinal disease characteristic of that due to diabetes. The coincidence of these two diabetic complications appears to him to be more than fortuitous. Acceptable evidence of occlusive arterial disease in patients with diabetic neuropathy was not unduly frequent. McKittrick and Root<sup>47</sup> have likewise noted the presence of neuritis in a considerable percentage of patients with lesions of the lower extremities in the absence or notable lack of vascular disease.

Deficiencies of vitamins were not observed, and the therapeutic use of vitamins, especially the vitamin B complex, was not found useful. This fact corroborates Jordan's<sup>42</sup> detailed study of 63 patients, in only 1 of whom the diet appeared to have been deficient. Rundles further states that a number of recent patients who had been given no vitamin supplements appeared to be recovering from their neuropathy as rapidly as had any others in the past, and adds that he has never seen clinical improvement in diabetic neuropathy by any treatment regimen in the absence of effective diabetic control.

The diagnosis of diabetic neuropathy is one of the least precise, because it is easy to ignore the muscular weakness, aches and pains of acute diabetic non-regulation, particularly if the neurologic examination is inexperienced. All that Rundles writes along these lines emphasizes the importance of an article by the late Dr Abraham Rudy,<sup>48</sup> in which he reports numerous cases of neuropathy in old-aged diabetic patients who were returned to well-being by the application of prolonged diabetic care and control of their disease.

The prognosis in diabetic neuropathy varies according to the severity of the neuritic disease. Recovery may take place within a few weeks or in six to twelve months, and in severe cases it may require one or two years.

In conclusion, Rundles points out the following

Occlusive arterial disease, diabetic cataracts, and advanced stages of diabetic retinopathy are late complications representing irreversible organic changes, which diabetic treatment will not alleviate and for which other treatment offers but poor compensation. Neuropathy, along with early stages of retinopathy and hepatomegaly, should be emphasized as reversible diabetic complications always a warning to both physician and patient of inadequately controlled diabetes which in the course of time, if uncorrected, will lead to widespread and permanent degenerative changes. At least 50 per cent of all diabetics will survive with little or no treatment for many years. In them the ultimate development of degenerative complications is the only criterion by which the adequacy of their treatment can be judged.

This article by Rundles is one of the most important in recent years, since it proves the necessity for painstaking and aggressive treatment of diabetes from its incipency to its very end

(To be concluded)

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32131

#### PRESENTATION OF CASE

A sixty-nine-year-old housewife entered the hospital in collapse

On the morning of admission she had an attack of excruciating substernal and epigastric pain and collapse lasting nearly an hour and followed by a loose bowel movement Three hours later, in the early afternoon, she was well enough to attempt to stoke the household furnace While at this task she had a second attack of upper abdominal pain, severer than the first The pain radiated to the left shoulder She apparently collapsed and was found lying on the floor about five hours later and was brought to the hospital

About five years before admission the patient had had an episode of deep right chest pain radiating to the scapula This attack was said to have been initiated by exercise and relieved by rest In the following years she had had attacks of epigastric pain approximately every six months, it began as a squeezing, nonradiating pain followed by nausea, vomiting and syncope for one to three hours There were no intervening symptoms She had known that she had hypertension for an indefinite number of years There had been no exertional dyspnea or ankle edema Many years previously she had had an ovary and a "tumor" removed from the abdomen

On physical examination the patient was cyanotic and responded poorly The apical impulse was not visible, and the left border of cardiac dullness was poorly defined, although it appeared to be just outside the midclavicular line The heart sounds were distant and at times were not heard There was moderate dullness over the left chest posteriorly from the spine to the posterior axillary line Breath sounds were diminished over this area There was severe epigastric tenderness without spasm No abdominal masses were palpated There was an old longitudinal midline scar above the symphysis Rectal examination was negative

The temperature was 97°F, the pulse 98, and the respirations 25 The blood pressure was unobtainable

The red-cell count was 4,020,000, with a hemoglobin of 8.5 gm, and the white-cell count 14,100 The urine had a specific gravity of 1.020, and the sediment contained 1 or 2 red cells and 15 to 20 white cells per high-power field A glove specimen of stool was guaiac negative The serum amylase was 29 units, and the nonprotein nitrogen 26 mg per 100 cc A portable x-ray film of the chest showed poor visualization of the left half of the diaphragm The heart was enlarged, and there was marked enlargement of the aorta

On the morning after admission the patient was more alert and her abdominal pain had lessened She had developed a severe productive cough, and the white-cell count rose to 25,900 There was no change in the temperature or pulse With plasma and saline the blood pressure rose to 80 systolic, 60 diastolic At 7.50 p.m. the same day she had a sudden severe pain under the right scapula and in the right axilla The blood pressure fell slightly but soon rose to 120 systolic, 70 diastolic At 8.20 p.m. she had another attack of excruciating pain in the same region and suddenly died

#### DIFFERENTIAL DIAGNOSIS

DR ALLAN G BRAILEY It seems to me that this woman died of cardiovascular disease One might think in passing of acute pancreatitis, but when she came to the hospital the serum amylase was found to be normal and the subsequent course seems completely inconsistent with pancreatitis Pulmonary embolism deserves attention The pain of embolism, however, is not so agonizing as that described here Embolism of such degree as to cause collapse would produce marked dyspnea, and there is no mention of evidence of dilatation of the right heart, such as distended neck veins There is no hint of a likely source of emboli, although the source is frequently obscure There is no mention of bloody sputum I do not believe that we need to suppose she had embolism as a primary cause of death

The two diagnoses that have to be carefully juxtaposed are myocardial infarction and dissecting aneurysm The story is consistent with infarction The patient was sixty-nine years old and was therefore likelier to die of coronary disease than of dissecting aneurysm Five years previously she had had chest pain brought on by effort and which may have been evidence of pre-existing coronary disease The heart signs and blood pressure are apt to be well maintained in dissecting aneurysm This patient, however, was obviously in shock when she came in, and the poor quality of the heart sounds and blood pressure could be as logically ascribed to shock as to the underlying condition The location of the pain was substernal and upper abdominal Three hours later the second attack was said to have been epigastric It is a good story for myocardial infarction but pain proceeding downward constitutes one argument in favor of dissecting

aneurysm There was no pericardial friction rub Of course that frequently is not present even with massive cardiac infarction An electrocardiogram would be a great help Was one taken?

DR TRACY B MALLORY No

DR BRAILEY It seems unlikely that a person three hours after severe infarction would feel like getting up and stoking a furnace

DR ROBERT L BERG A cardioscope was taken in the Emergency Ward and was negative

DR BRAILEY The fact that she made a temporary recovery to the point where she was willing to stoke the furnace suggests that her attack was due to dissecting aneurysm She was known to have hypertension for years, a constant prerequisite for dissection The character of the onset of the pain in these cases is usually significant, but we cannot be too sure what it was like here If it came on suddenly, it would favor aneurysm The pain of cardiac infarction comes on over a period of a few minutes If she had a dissecting aneurysm, the terminal episode of pain in the right chest might have resulted from dissection upward Four seizures of terrific pain in twenty-four hours favor an aneurysm with discontinuous dissection It is not likely that she had four such closely repeated infarctions of the heart Somewhat against dissection is the report that the blood pressure stayed low If it did stay low, we have to assume that this was due to a state of shock It may be significant that the last two attacks of pain occurred only after the blood pressure began to rise A more serious objection is the fact that no evidence is given of occlusion of the branches of the aorta, but some of the intercostal branches might have been occluded without producing obvious symptoms in so sick a patient

Are there any x-ray films?

DR MILFORD D. SCHULZ The film has been lost

DR BRAILEY I should like to know particularly about the aorta If it was enlarged it might easily have resulted from hypertension and arteriosclerosis I also wish I knew how big the right ventricle was Nothing is said about that

The patient died suddenly How sudden is "suddenly"? Instantaneous death from heart disease may be due to ventricular fibrillation, to cardiac standstill or to rupture of the heart or aorta, but she certainly had not had coronary occlusion long enough to have ruptured the heart She could easily have died of a disturbance of rhythm This is a difficult problem to decide, but I shall vote in favor of dissecting aneurysm and try to justify it on the basis that the pain moved downward, that she had four attacks of terrific pain of sudden onset and that death was instantaneous

DR MALLORY Dr Berg, will you tell us how the discussion ran on the wards?

DR BERG When she first came in she was seen in the Emergency Ward and was in coma No history was obtainable She was given intravenous

fluids and became somewhat responsive She had abdominal pain and was extremely tender in the epigastrium The chief problem was whether her condition represented an intra-abdominal catastrophe or something originating in the cardiovascular system The surgeons saw her at that time and agreed that there was no immediate need of surgical intervention, and as she improved we were able to get the rest of the story, which focused more closely on the cardiovascular system as time went on I personally did not see the x-ray film, but Dr John Stanbury, who admitted the patient, said that it showed a very much enlarged aorta She was sent up to the wards with a diagnosis of dissecting aneurysm

So far as the manner of death is concerned, I might add that after the last attack of pain she died within thirty seconds

DR CHARLES H BURNETT There was no question from the x-ray film that the aorta was markedly enlarged

DR MALLORY Does that alter your opinion, Dr Brailey?

DR BRAILEY No, it rather helps to confirm my diagnosis

DR ALBERT J STUNKARD The blood pressure, which was unobtainable in the Emergency Ward, was up the next morning

#### CLINICAL DIAGNOSES

Dissecting aortic aneurysm  
Arteriosclerotic heart disease  
Bronchopneumonia

#### DR BRAILEY'S DIAGNOSES

Dissecting aneurysm of aorta

#### ANATOMICAL DIAGNOSES

Ruptured syphilitic aneurysm of aorta  
Hematoma of mediastinum

#### PATHOLOGICAL DISCUSSION

DR MALLORY This patient showed a large fusiform aneurysm of the thoracic aorta, not a dissecting aneurysm, but I believe a syphilitic one, despite her advanced age Patients with syphilitic aneurysm do not ordinarily reach the age of sixty-nine The specimen grossly was strongly suggestive of syphilis, it showed wrinkling, so-called "tree barking" and stellate scarring of the intima Microscopically there were many foci of destruction in the media and also a marked perivascular cuffing with lymphocytes and occasional plasma cells, characteristic of syphilitic aortitis The aneurysm had ruptured, and a massive hematoma of the mediastinum had formed There was then dissection of this hematoma in various directions—upward to the base of the heart and downward into the serosa of the stomach, a large portion of which was lifted off the muscularis by the clotted blood

It is quite probable that the epigastric pain and tenderness were directly related to this last extension of blood. It had broken into one pleural cavity, where about 900 cc of fluid was found, about half of it consisting of blood clots.

It was not a true dissecting aneurysm because, as you know, in a dissecting aneurysm the separation in the aorta is within the media so that muscle fibers of the media are found on each side of the plane of dissection. Under such circumstances the pressure in the newly dissected vessel equals or exceeds that within the main aortic lumen, thus occluding by external pressure the small aortic branches. Dr Brailey looked for clinical evidence of this phenomenon in the record but could not find it.

### CASE 32132

#### PRESENTATION OF CASE

A seventy-year-old physician entered the hospital because of persistent vomiting.

Six months before admission the patient began to complain of epigastric fullness and indigestion. He restricted his diet to fluids and soft foods and in six months lost 20 pounds. Ten days prior to admission he had an attack of vomiting, with epigastric discomfort, the vomitus was foul smelling. He was constipated, and enema returns were slight.

On physical examination there was a soft non-tender mass in the left upper quadrant that extended from the rib margin to the level of the umbilicus and moved slightly with respiration. There was slight clubbing of the fingers.

The temperature was 98°F, the pulse 90, and the respirations 18. The blood pressure was 140 systolic, 90 diastolic.

The red-cell count was 4,300,000, and the white-cell count 12,200, with 75 per cent neutrophils. The urine had a specific gravity of 1.012, there was no albumin. The prothrombin time was 20 seconds (normal, 14 to 16 seconds), the nonprotein nitrogen 27 mg per 100 cc, the serum protein 6.1 gm, and the chloride 106 milliequiv per liter.

An x-ray film of the chest showed bright lung fields. Between unusually prominent pulmonary markings there were dispersed numerous rounded translucent areas. The appearance was consistent with pulmonary fibrosis with some cystic changes. An intravenous pyelogram revealed a tumor mass filling the left flank and kidney area, its outline was indefinite. There was no filling of the left kidney pelvis. The right kidney functioned normally. In a retrograde pyelogram, the left ureter filled throughout. It was small and swung to the right so that it crossed the spine at the fifth lumbar vertebra. The pelvis was flattened, rotated and lay almost to the right of the spine.

A gastrointestinal series taken on the eleventh hospital day showed that the stomach, colon and duodenum were deformed by an apparently ex-

trinsic mass on the left side. The stomach was displaced upward and anteriorly. The duodenal bulb was compressed toward the right. The ligament of Treitz was pressed forward and downward. The descending colon was displaced laterally, and the splenic flexure upward. There was barium in the stomach, terminal ileum and cecum twenty-four hours after the meal.

The patient had a slight fever on the thirteenth day, and there was tenderness in the left costo-vertebral region. These signs quickly disappeared. Another urine showed 10 to 15 white cells per high-power field, and on culture there was a moderate growth of *Staphylococcus albus*.

An operation was performed on the twenty-second hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR FLETCHER H COLBY: Since the diagnosis rests largely on the x-ray findings, I shall ask the roentgenologist to interpret the films now.

DR JAMES R LINGLEY: The chest shows a diffuse linear density throughout both lungs that is consistent with fibrosis. The hilar shadows are prominent and perhaps somewhat nodular. Incidentally, in cases of this type one should always think of diffuse pulmonary metastases. The plain abdominal film shows density throughout the left side of the abdomen, apparently due to a large mass the margins of which are not too well defined. On the retrograde film, there is displacement of the ureters to the right and the kidney pelvis is not well filled. In the intravenous pyelogram there is no evidence of excretion on the affected side. The gastrointestinal films show displacement of the stomach to the right and some displacement of the descending colon.

DR COLBY: Is the pulmonary picture consistent with metastases?

DR LINGLEY: I think it is more consistent with fibrosis, but metastatic disease is a possibility.

DR COLBY: The x-ray report states that the renal pelvis on the affected side was flattened and rotated. That is an important finding, but I suggest that the irregularity in this region represents ureter and not renal pelvis.

DR LINGLEY: I believe that you are correct. The pelvis is probably not filled on the affected side.

DR COLBY: Are these x-ray findings in the gastrointestinal tract — the displacement of the stomach, duodenum and large bowel — quite consistent with a tumor arising from the right kidney?

DR LINGLEY: I believe that the mass is a greatly enlarged left kidney.

DR COLBY: We have a patient seventy years of age who had had gastrointestinal symptoms for at least six months. He had had persistent vomiting for the ten days before entry. On examination there was found a large mass that filled the left loin and extended down almost to the pelvis on that side. From the x-ray study with pyelograms, intravenous



aneurysm There was no pericardial friction rub Of course that frequently is not present even with massive cardiac infarction An electrocardiogram would be a great help Was one taken?

DR TRACY B MALLORY No

DR BRAILEY It seems unlikely that a person three hours after severe infarction would feel like getting up and stoking a furnace

DR ROBERT L BERG A cardioscope was taken in the Emergency Ward and was negative

DR BRAILEY The fact that she made a temporary recovery to the point where she was willing to stoke the furnace suggests that her attack was due to dissecting aneurysm She was known to have hypertension for years, a constant prerequisite for dissection The character of the onset of the pain in these cases is usually significant, but we cannot be too sure what it was like here If it came on suddenly, it would favor aneurysm The pain of cardiac infarction comes on over a period of a few minutes If she had a dissecting aneurysm, the terminal episode of pain in the right chest might have resulted from dissection upward Four seizures of terrific pain in twenty-four hours favor an aneurysm with discontinuous dissection It is not likely that she had four such closely repeated infarctions of the heart Somewhat against dissection is the report that the blood pressure stayed low If it did stay low, we have to assume that this was due to a state of shock It may be significant that the last two attacks of pain occurred only after the blood pressure began to rise A more serious objection is the fact that no evidence is given of occlusion of the branches of the aorta, but some of the intercostal branches might have been occluded without producing obvious symptoms in so sick a patient

Are there any x-ray films?

DR MILFORD D SCHULZ The film has been lost

DR BRAILEY I should like to know particularly about the aorta If it was enlarged it might easily have resulted from hypertension and arteriosclerosis I also wish I knew how big the right ventricle was Nothing is said about that

The patient died suddenly How sudden is "suddenly"? Instantaneous death from heart disease may be due to ventricular fibrillation, to cardiac standstill or to rupture of the heart or aorta, but she certainly had not had coronary occlusion long enough to have ruptured the heart She could easily have died of a disturbance of rhythm This is a difficult problem to decide, but I shall vote in favor of dissecting aneurysm and try to justify it on the basis that the pain moved downward, that she had four attacks of terrific pain of sudden onset and that death was instantaneous

DR MALLORY Dr Berg, will you tell us how the discussion ran on the wards?

DR BERG When she first came in she was seen in the Emergency Ward and was in coma No history was obtainable She was given intravenous

fluids and became somewhat responsive She had abdominal pain and was extremely tender in the epigastrium The chief problem was whether her condition represented an intra-abdominal catastrophe or something originating in the cardiovascular system The surgeons saw her at that time and agreed that there was no immediate need of surgical intervention, and as she improved we were able to get the rest of the story, which focused more closely on the cardiovascular system as time went on I personally did not see the x-ray film, but Dr John Stanbury, who admitted the patient, said that it showed a very much enlarged aorta She was sent up to the wards with a diagnosis of dissecting aneurysm

So far as the manner of death is concerned, I might add that after the last attack of pain she died within thirty seconds

DR CHARLES H BURNETT There was no question from the x-ray film that the aorta was markedly enlarged

DR MALLORY Does that alter your opinion, Dr Brailey?

DR BRAILEY No, it rather helps to confirm my diagnosis

DR ALBERT J STUNKARD The blood pressure, which was unobtainable in the Emergency Ward, was up the next morning

#### CLINICAL DIAGNOSES

Dissecting aortic aneurysm  
Arteriosclerotic heart disease  
Bronchopneumonia

#### DR BRAILEY'S DIAGNOSES

Dissecting aneurysm of aorta

#### ANATOMICAL DIAGNOSES

Ruptured syphilitic aneurysm of aorta  
Hematoma of mediastinum

#### PATHOLOGICAL DISCUSSION

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DR COLBY: We have a patient seventy years of age who had had gastrointestinal symptoms for at least six months. He had had persistent vomiting for the ten days before entry. On examination there was found a large mass that filled the left loin and extended down almost to the pelvis on that side. From the x-ray study with pyelograms, intravenous

and retrograde, I think it is fair to say that the mass was definitely localized in the left kidney and was presumably a tumor mass arising from that organ. It is not at all unusual to have gastrointestinal symptoms predominant from renal disease, although they are usually caused by right-sided lesions. These symptoms are regarded as being due either to involvement of the sympathetic nerves that supply the gastrointestinal tract, such as occurs in malignant disease, or to pressure of the enlarged kidney on the adjacent organs. The foul vomitus, the pressure defects on the stomach and duodenum, the displacement of the large bowel and the retention of barium lead one to think that the gastrointestinal symptoms were simply due to pressure from the large left-sided renal mass, particularly since no intrinsic lesion of the gastrointestinal tract was demonstrated.

The essential problem is to determine the nature of the left-sided renal mass. The possibilities to consider are a solid tumor arising from the renal parenchyma, a tumor of the renal pelvis with retention within the kidney, a large solitary cyst of the kidney and hydronephrosis.

So far as a solid tumor is concerned, there are several points that seem to be against it. In the first place, there was lack of bleeding. A single urine examination is recorded, but there were only a few white cells and no red cells. Solid tumors of the kidney, however, can go a long time without either gross or microscopic bleeding. Also against a solid tumor is the fact that the mass was described as being soft. Tumors of the renal parenchyma are firm and hard. The surgeon is frequently uncertain whether a mass involving a kidney is solid or cystic until operation. It seems unlikely, however, that this was a solid tumor. To me the x-ray findings are not characteristic of metastatic disease in the lung.

Tumors of the renal pelvis bleed early and often. This was not the case in this patient.

A solitary cyst of the kidney is a distinct possibility, but we have no definite information that would lead us to believe that this was a solitary cyst. In a solitary cyst there is usually a distinct rounded filling defect of the renal pelvis, which is extremely suggestive and sometimes quite characteristic. We lack that evidence here.

Hydronephrosis seems to be the likeliest cause of this large soft mass. The patient had had no pain,

but this can be explained by the slow development of the hydronephrosis. There had been no pain suggestive of calculus, and there is no shadow of stone by x-ray. There is, of course, a possibility of a non-opaque stone, but the fact that the patient had had no attacks of pain in the past is somewhat against this. The most probable cause of the hydronephrosis seems to be obstruction at the ureteropelvic junction, although the actual lesion is frequently not demonstrable at the time of operation.

DR TRACY B. MALLORY: Are there any suggestions or questions?

DR W. WILSON SCHIER: Could a retroperitoneal lipoma fit this picture?

DR COLBY: I have had little experience with retroperitoneal lipomas.

DR MALLORY: Dr Smith, will you tell us about your operative findings?

DR GEORGE G. SMITH: This patient had a large hydronephrosis, which extended well across the midline and seemed to push directly against the lower part of the stomach. There was nothing particularly remarkable about it. I do not remember whether the obstruction was at the ureteropelvic junction.

DR MALLORY: The operative note mentions a double pedicle. Would that suggest that aberrant vessels might have been the cause of the hydronephrosis?

DR SMITH: It might, but I do not know.

#### CLINICAL DIAGNOSIS

Cyst of left kidney

#### DR COLBY'S DIAGNOSIS

Hydronephrosis left kidney

#### ANATOMICAL DIAGNOSIS

Hydronephrosis left kidney.

#### PATHOLOGICAL DISCUSSION

DR MALLORY: What this hydronephrosis had to do with the patient's major symptoms, which were gastrointestinal, remains a problem. From the postoperative record it is evident that he was not relieved of the gastrointestinal symptoms by the removal of the kidney. Repeated x-ray examinations showed persistent gastric stasis, and eventually the stomach was explored by Dr L. S. McKittrick. He was unable to find any organic obstruction but nevertheless did a pyloroplasty, with some degree of relief.

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## MERGER AND MEDICAL SERVICE

THERE has been considerable interest and excitement in recent months about the proposed merger of the armed forces in this country. The obvious advantages from the point of view of efficiency and the importance of co-ordinated effort by all branches of the armed forces in modern warfare have been widely discussed. The resistance to such a merger by those who suspect that their branch might become subordinated in the course of such a merger is, of course, understandable. Nevertheless, the Secretary of the Navy has recently announced that plans are being drawn up and action is already being taken for the merging of several types of facilities that are now duplicated in the Army and Navy. This

is the first departure during peacetime from the traditional and not always good-natured rivalry between the different branches of the service. Arrangements are already being made for merging or co-ordinating activities of Army and Navy facilities in matters concerning procurement, intelligence, ports and shipping, air transport services and even recruiting and training.

No specific mention was made in this announcement about the merging of the medical departments of the services, but that is obviously an important function that could easily benefit by some sort of co-ordination and, probably better still, by complete unification. Although it may sound quite radical, it might not even be amiss to consider the possibility of removing the medical services entirely from the armed forces during peacetime, running them in conjunction with existing civilian institutions.

A good deal has appeared both in the medical and in the lay press about the superior quality of the medical services that were rendered to the armed forces during the war. The low case-fatality rates and the improved cure rates, as compared with those obtained in similar conditions during the last war, are always quoted as proof of this contention. Much of this improvement in end results, however, can readily be ascribed to technics and to life-saving therapeutic measures that had been evolved after the end of World War I but before the beginning of this war. In spite of this, there are still discrepancies between civilian and military practice that leave much to be desired.

One naturally expects the medical services of the armed forces to provide the best and most modern forms of treatment and care. Whether the actual accomplishments during this war are uniformly of as high a quality as one has been led to believe is open to question. Obviously open criticism of the services by officers while they are on active duty is well nigh impossible. In private, however, many of them have been quite vocal in their condemnation of many features of these services. It is to be hoped that, now that the war is over, their criticisms can be aired, and that the causes of any justifiable complaints can be ferreted out and corrected. Many physicians of high professional caliber have seen active service in all branches of the armed forces

Some of them were fortunate, having had the opportunity to utilize their skills to the fullest. Others of equal attainment spent most of their time in "paper work," while holding rather exalted ranks, and still others were treated much as enlisted men, being ordered to do menial duties without any reference to their skills and training. When these officers return to a civilian status, they may prefer to forget their gripes and to get back to their jobs, but they can render an important service by presenting and analyzing their observations and criticisms, unhampered by service regulations.

There are undoubtedly many features of medical service that could be improved as a result of the merging of the medical branches of the armed forces. A uniform and, it is hoped, better policy concerning appointments and assignments to duties based on experience and skill could well be instituted. The services and advice of leading medical authorities could then be better utilized than they have been in the past. A co-ordination of hospital and other facilities for the best management of all types of medical problems, as well as for research, would also accrue to the benefit of all the services. In setting up a new medical department, provision could be made for co-ordinating its activities with those of established medical centers, particularly, although not exclusively, those connected with teaching hospitals and medical schools, much in the same manner as is now being contemplated for the Veterans Administration. Inspiration derived from medical teachers, from those actively engaged in research and perhaps even from collaboration in research activities would help maintain the morale of the medical officers who elect to remain in service.

#### ALBRECHT VON HALLER — PHYSICIAN-EXTRAORDINARY

ALBRECHT VON HALLER was born at Berne, Switzerland, on October 16, 1708. It is reported that when he was ten years of age he could speak Latin, Greek, Hebrew and Chaldaic, having written verses in Latin, dictionaries for the Greek and Hebrew and a grammar for Chaldean. He studied medicine at Tübingen under Cavernarius and then at Leyden

under Boerhaave and Albinus, receiving his medical degree at nineteen, after submitting a thesis that proved that the so-called "salivary duct" claimed as a discovery by Coschwitz was a simple blood vessel.

He traveled for two years, visiting the University of Paris and the University of London, and then returned to Switzerland to study botany at Basle. He began a collection of plants that became the basis of his tremendous work on plant classification and Swiss flora published in 1742. In his spare time he wrote stories and verses. One of his poems, "*Die Alpen*," is still found in the anthologies.

Von Haller then returned to Berne, where for seven years he engaged in general practice. He applied for the post of city physician but was rejected with the comment "He is a poet. Why should he want to be a hospital physician?"

At the age of twenty-eight, his growing fame as a botanist and an anatomist led to his appointment by George II to the chair in botany, anatomy, surgery and medicine at the newly founded University of Göttingen, and during the next seventeen years he demonstrated a productivity of scientific research and study that has probably never been equaled. He lectured on the subjects covered in his appointment and in addition wrote a history of medicine, the first textbook of physiology, an atlas of angiology, one on pathology and the volume on the classification of plants previously mentioned. In original research he proved that muscle irritability was independent of nerve supply, that bile was concerned with fat digestion, that the pleural cavities contained no air, and that the heart beat was automatic in origin. He described the development of the embryo and the anatomy of the organs of generation and of the brain. In addition, he accurately explained the mechanism of respiration.

Von Haller founded the *Göttingische gelehrte Anzeigen*, a monthly journal, to which he contributed the almost unbelievable total of twelve thousand papers on almost every branch of knowledge. He continued to write verse and published several historical novels. It is difficult to envisage the circumstances under which this work was done, since it should be remembered that the time was the early

eighteenth century, thirty years before the Revolutionary War

In 1753, at the age of forty-five, he returned to Berne, where in the next twenty-five years he occupied several municipal and state offices. He prepared his *Bibliotheca medica*, of which he completed the botanical, anatomical, surgical and medical portions, a work that fills ten quarto volumes. He re-wrote his elements of physiology in four quarto volumes. He continued his nonmedical writing and published a history of Alfred the Great and two other philosophical romances, *Usonia* (1771) and *Fabius und Cato* (1774). He continued his classical studies by writing commentaries on Greek and Latin texts. With all this, until his death in 1777, he found time and energy to carry on a voluminous correspondence with the great scientists of his day.

Although the most famous surgeon of his time he would not operate on human beings. So great was his fame that some pirates who captured an English ship and found on it a package of books directed to him, considered it a crime to rob so learned a man and hurried to the nearest port in order that the books might reach him as soon as possible.

Von Haller was undoubtedly one of the most extraordinary men to grace the profession of medicine, yet he receives scant recognition in modern medical textbooks. Many anatomies do not associate his name with one of his important discoveries,—the vas aberrans,—and the majority of textbooks on physiology do not refer to him at all.

## MASSACHUSETTS MEDICAL SOCIETY

### SPECIAL MEETING OF THE COUNCIL

A special meeting of the Council of the Massachusetts Medical Society will be held in Boston on Wednesday, April 10, 1946, at 10:30 a.m., in Building E, Harvard Medical School, Longwood Avenue.

*Business*  
1 Report of the Committee Appointed to Confer With Major General Hawley, Medical Administrator of the Veterans Administration, concerning the medical care of veterans by civilian physicians.

2 Schedule to cover fees for services under this heading.

MICHAEL A. TIGHE, M.D., Secretary

Building E is the first building on the right when the quadrangle of the Medical School is entered from Longwood Avenue. Councilors are asked to sign one of the attendance books before the meeting. The Cotting luncheon will be served at 1:00 p.m. in the Dining Room of Vanderbilt Hall.

## SECRETARY'S OFFICE

### SURPLUS PROPERTY FOR VETERAN MEDICAL OFFICERS

Few discharged medical officers appreciate the fact that they are entitled to a priority in the purchase of surplus medical equipment, when, as and if it is available, and the majority of those who are aware of this fact have no idea concerning what steps to take in purchasing such equipment.

All who intend to apply must first obtain certification from one of the district offices of the War Assets Corporation. Four such offices are located in Massachusetts, as follows:

<i>Boston</i>	<i>Lowell</i>
Henry Boltz, district manager	E. J. Moriarty, acting district manager
1 Court Street	8 Merrimack Street
Tel. LA Fayette 7500	Tel. Lowell 6388
<i>Springfield</i>	<i>Worcester</i>
Lee Manley, district manager	G. W. Grebenstein, district manager
1200 Main Street	340 Main Street
Tel. Springfield 3-7857	Tel. Worcester 6-4391

At such an office, on presentation of his orders for separation under honorable conditions and his certification that the equipment is for use in his own professional enterprise, the veteran's application for the described property is approved on Form 66. He retains one copy, for use at the time of inspection or purchase of what he desires, and the other copy is forwarded to the appropriate disposal agency, which in the case of New England purchasers of medical equipment is the Consumer Goods Division, War Assets Corporation, 600 Washington Street, Boston. When this disposal station has acquired enough material to make a sale worth while, those veterans interested in the type of goods to be sold will be sent a catalogue, giving the stock number, Army nomenclature and price of the material offered and place where it may be inspected prior to the sale.

The veteran may be present in person at the sale or he may write to the disposal agency, giving his case number (from Form 66), applying for whatever articles he desires to purchase and enclosing a certified check. An opportunity to inspect the various items that are offered for sale may or may not be given, depending on the location of the stock. The sale to veterans will extend over a period of about two weeks on each lot offered.

To avoid disappointment, veterans should realize that they do not have the first choice on these goods. The first priority goes to federal agencies, and the second priority to agencies of a state, county or municipality. After these purchasers have been satisfied, the veteran has his chance, and what is then left is offered to nonprofit institutions, such as hospitals, and finally to the public. There is a movement on foot in the Congress to move the veteran doctor from the third priority class to the second.

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#### ALBRECHT VON HALLER — PHYSICIAN-EXTRAORDINARY

ALBRECHT VON HALLER was born at Berne, Switzerland, on October 16, 1708. It is reported that when he was ten years of age he could speak Latin, Greek, Hebrew and Chaldaic, having written verses in Latin, dictionaries for the Greek and Hebrew and a grammar for Chaldee. He studied medicine at Tübingen under Cavernarius and then at Leiden

under Boerhaave and Albinus, receiving his medical degree at nineteen, after submitting a thesis that proved that the so-called "salivary duct" claimed as a discovery by Coschwitz was a simple blood vessel.

He traveled for two years, visiting the University of Paris and the University of London, and then returned to Switzerland to study botany at Basle. He began a collection of plants that became the basis of his tremendous work on plant classification and Swiss flora published in 1742. In his spare time he wrote stories and verses. One of his poems, "*Die Alpen*," is still found in the anthologies.

Von Haller then returned to Berne, where for seven years he engaged in general practice. He applied for the post of city physician but was rejected with the comment "He is a poet. Why should he want to be a hospital physician?"

At the age of twenty-eight, his growing fame as a botanist and an anatomist led to his appointment by George II to the chair in botany, anatomy, surgery and medicine at the newly founded University of Göttingen, and during the next seventeen years he demonstrated a productivity of scientific research and study that has probably never been equaled. He lectured on the subjects covered in his appointment and in addition wrote a history of medicine, the first textbook of physiology, an atlas of angiology, one on pathology and the volume on the classification of plants previously mentioned. In original research he proved that muscle irritability was independent of nerve supply, that bile was concerned with fat digestion, that the pleural cavities contained no air, and that the heart beat was automatic in origin. He described the development of the embryo and the anatomy of the organs of generation and of the brain. In addition, he accurately explained the mechanism of respiration.

Von Haller founded the *Göttingische gelehrte Anzeigen*, a monthly journal, to which he contributed the almost unbelievable total of twelve thousand papers on almost every branch of knowledge. He continued to write verse and published several historical novels. It is difficult to envisage the circumstances under which this work was done, since it should be remembered that the time was the early

eighteenth century, thirty years before the Revolutionary War

In 1753, at the age of forty-five, he returned to Berne, where in the next twenty-five years he occupied several municipal and state offices. He prepared his *Bibliotheca medica*, of which he completed the botanical, anatomical, surgical and medical portions, a work that fills ten quarto volumes. He rewrote his elements of physiology in four quarto volumes. He continued his nonmedical writing and published a history of Alfred the Great and two other philosophical romances, *Usonia* (1771) and *Fabius und Cato* (1774). He continued his classical studies by writing commentaries on Greek and Latin texts. With all this, until his death in 1777, he found time and energy to carry on a voluminous correspondence with the great scientists of his day.

Although the most famous surgeon of his time he would not operate on human beings. So great was his fame that some pirates who captured an English ship and found on it a package of books directed to him, considered it a crime to rob so learned a man and hurried to the nearest port in order that the books might reach him as soon as possible.

Von Haller was undoubtedly one of the most extraordinary men to grace the profession of medicine, yet he receives scant recognition in modern medical textbooks. Many anatomies do not associate his name with one of his important discoveries,—the vas aberrans,—and the majority of textbooks on physiology do not refer to him at all.

## MASSACHUSETTS MEDICAL SOCIETY

### SPECIAL MEETING OF THE COUNCIL

A special meeting of the Council of the Massachusetts Medical Society will be held in Boston on Wednesday, April 10, 1946, at 10 30 a m, in Building E, Harvard Medical School, Longwood Avenue.

*Business*  
1 Report of the Committee Appointed to Confer With Major General Hawley, Medical Administrator of the Veterans Administration, concerning the medical care of veterans by civilian physicians.

2 Schedule to cover fees for services under this heading.

MICHAEL A. TIGHE, M D, Secretary

Building E is the first building on the right when the quadrangle of the Medical School is entered from Longwood Avenue.  
Councilors are asked to sign one of the attendance books before the meeting. The Cotting luncheon will be served at 1:00 p m in the Dining Room of Vanderbilt Hall.

## SECRETARY'S OFFICE

### SURPLUS PROPERTY FOR VETERAN MEDICAL OFFICERS

Few discharged medical officers appreciate the fact that they are entitled to a priority in the purchase of surplus medical equipment, when, as and if it is available, and the majority of those who are aware of this fact have no idea concerning what steps to take in purchasing such equipment.

All who intend to apply must first obtain certification from one of the district offices of the War Assets Corporation. Four such offices are located in Massachusetts, as follows:

<i>Boston</i>	<i>Lowell</i>
Henry Boltz, district manager	E J Moriarty, acting district manager
1 Court Street	8 Merrimack Street
Tel LA Fayette 7500	Tel Lowell 6388
<i>Springfield</i>	<i>Worcester</i>
Lee Manley, district manager	G W Grebenstein, district manager
1200 Main Street	340 Main Street
Tel Springfield 3-7857	Tel Worcester 6-4391

At such an office, on presentation of his orders for separation under honorable conditions and his certification that the equipment is for use in his own professional enterprise, the veteran's application for the described property is approved on Form 66. He retains one copy, for use at the time of inspection or purchase of what he desires, and the other copy is forwarded to the appropriate disposal agency, which in the case of New England purchasers of medical equipment is the Consumer Goods Division, War Assets Corporation, 600 Washington Street, Boston. When this disposal station has acquired enough material to make a sale worth while, those veterans interested in the type of goods to be sold will be sent a catalogue, giving the stock number, Army nomenclature and price of the material offered and place where it may be inspected prior to the sale.

The veteran may be present in person at the sale or he may write to the disposal agency, giving his case number (from Form 66), applying for whatever articles he desires to purchase and enclosing a certified check. An opportunity to inspect the various items that are offered for sale may or may not be given, depending on the location of the stock. The sale to veterans will extend over a period of about two weeks on each lot offered.

To avoid disappointment, veterans should realize that they do not have the first choice on these goods. The first priority goes to federal agencies, and the second priority to agencies of a state, county or municipality. After these purchasers have been satisfied, the veteran has his chance, and what is then left is offered to nonprofit institutions, such as hospitals, and finally to the public. There is a movement on foot in the Congress to move the veteran doctor from the third priority class to the second.

MICHAEL A. TIGHE, M D, Secretary



## REVIEW LECTURE COURSE

Two changes have been made in the program of the Postgraduate Review Lecture Course recently forwarded to all registered physicians in Massachusetts

In the first place, the time of the meeting on Wednesday, May 8, has been changed, the four speakers beginning their talks at 3 00, 3 45, 4 30 and 5 15, respectively

Secondly, the title of the exercise on Monday, May 13, has been changed from "Round-Table Discussion on Obstetrics in General Practice" to "A Critical Review of Progress in Obstetrics during the Last Four Years, including a Consideration of Certain Immediate Problems of the Newborn"

MASSACHUSETTS DEPARTMENT  
OF PUBLIC HEALTHCOMMUNICABLE DISEASES IN  
MASSACHUSETTS FOR FEBRUARY, 1946

## RÉSUMÉ

DISEASES	FEBRUARY 1946	FEBRUARY 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	1	3	0
Chancroid	1	1	*
Chicken pox	764	1340	1347
Diphtheria	21	14	12
Dog bite	503	497	531
Dysentery, bacillary	9	9	12
German measles	216	116	116
Gonorrhea	494	303	303
Granuloma inguinale	0	0	*
Lymphogranuloma venereum	1	3	*
Malaria	102	53	1
Measles	1141	305	1876
Meningitis, meningococcal	21	21	12
Meningitis, Pfeiffer bacillus	2	3	2
Meningitis, pneumococcal	4	2	4†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	0	0	0†
Meningitis undetermined	3	6	6†
Mumps	639	1888	1091
Pneumonia lobar	224	241	461
Salmonella infections	8	4	3
Scarlet fever	707	1201	1201
Syphilis	526	351	363
Tuberculosis pulmonary	218	192	179
Tuberculosis other forms	11	14	14
Typhoid fever	1	2	3
Undulant fever	0	1	2
Whooping cough	411	595	658

\*Made reportable December 1943

†Four-year average

## COMMENT

Measles, this month, showed a fourfold increase over last year's near record low. Mumps reached its lowest February figure in 10 years. Chicken pox was at its lowest since 1929.

Record low figures were reported for lobar pneumonia and tuberculosis, other forms.

The first cases of typhoid and anterior poliomyelitis for the current year were reported during February.

## GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Stoughton, 1, total, 1.

Diphtheria was reported from Arlington, 1, Boston, 7, Camp Edwards, 1, Gloucester, 2, Haverhill, 1, Lynn, 1, Malden, 1, Somerville, 2, Southampton, 1, Springfield, 1, Taunton, 2, Wellfleet, 1, total, 21.

Dysentery, amebic, was reported from Cambridge, 1, Revere, 1, Waltham (Regional Hospital), 1, total, 3.

Dysentery, bacillary, was reported from Marblehead, 3, Wrentham (State School), 6, total, 9.

Hookworm was reported from Camp Edwards, 1, total, 1.

Malaria was reported from Athol, 1, Bedford, 1, Belmont, 1, Beverly, 1, Boston, 17, Braintree, 1, Brockton, 1, Brookline, 1, Cambridge, 2, Camp Edwards, 7, Chelsea, 1, Dedham, 1, Everett, 2, Franklin, 1, Gardner, 2, Haverhill, 1,

Holbrook, 3, Leicester, 1, Leominster, 1, Lynn, 2, Lynnfield, 1, Malden, 3, Marblehead, 1, Marlboro, 2, Medford, 1, Melrose, 1, Methuen, 1, Milton, 1, Norwood, 2, Peabody, 4, Quincy, 2, Revere, 1, Rowley, 1, Salem, 1, Saugus, 1, Somerset, 1, Somerville, 3, Springfield, 2, Taunton, 2, Tyngsboro, 1, Wakefield, 1, Walpole, 1, Waltham, 2, Waltham Regional Hospital, 10, Wellesley, 1, Wilmington, 1, Worcester, 6, total, 102.

Meningitis, meningococcal, was reported from Boston, 4, Braintree, 1, Cambridge, 1, Everett, 1, Fall River, 3, Framingham, 1, Gloucester, 1, Leominster, 1, Lexington, 1, Milford, 1, Newton, 1, Southbridge, 1, Taunton, 1, Waltham, 1, Waltham Regional Hospital, 1, Worcester, 1, total, 21.

Meningitis, Pfeiffer bacillus, was reported from Fallmouth, 1, New Bedford, 1, total, 2.

Meningitis, pneumococcal, was reported from Boston, 1, Cambridge, 1, Everett, 1, Framingham, 1, total, 4.

Meningitis, undetermined, was reported from Cambridge, 1, Westfield, 2, total, 3.

Salmonella infections were reported from Brockton, 1, Cambridge, 4, Fitchburg, 1, Holyoke, 1, Norwood, 1, total, 8.

Septic sore throat was reported from Barre, 1, Boston, 7, Haverhill, 2, Merrimack, 2, North Adams, 1, Salem, 1, total, 14.

Tetanus was reported from Fall River, 1, total, 1.

Trichinosis was reported from Danvers, 1, Somerville, 1, Westport, 2, total, 4.

Typhoid fever was reported from Malden, 1, total, 1.

CONSULTATION CLINICS FOR CRIPPLED  
CHILDREN IN MASSACHUSETTS UNDER  
THE PROVISIONS OF THE SOCIAL  
SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	April 1	Paul W. Hugenberger
Haverhill	April 3	William T. Green
Lowell	April 5	Albert H. Brewster
Brockton	April 11	George W. Van Gorder
Pittsfield	April 15	Frank A. Slowick
Springfield	April 16	Garry deN. Hough, Jr.
Fall River	April 22	David S. Grice
Hyannis	April 23	Paul L. Norton
Worcester	April 26*	John W. O'Meara

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments.

\*Day changed

## CORRESPONDENCE

## A PLEA FOR THE GENERAL PRACTITIONER

To the Editor: Looking back over more than twenty-five years of general practice, with all their rough spots, as well as their smooth and pleasant ones, I feel grieved that the term "general practitioner," with its broad but plebeian meaning, has had no chance to lift itself from its lowly stratum in the medical world. How often the phrase, "He is a great specialist!" Has anyone ever heard, by chance, a remark such as, "It is remarkable how many things Dr. — can do, and do well"? It is certainly seldom uttered by a fellow physician, and a layman never makes the remark with the same sure confidence with which he tells the world "Dr. — is going to operate on my wife. He is a fellow of the American College of Surgeons." Hence my thesis, Why not an American College of General Practitioners?

What percentage of medical men are general practitioners? I certainly believe that they compose the majority. The economic exigencies of rural medicine make this statement sure. Throughout the history of medicine, it has been commonly recognized that general practitioners form the largest and most important subdivision of medical practice.

It is also true, that this group has furnished many men who have become outstanding in the medical world. We are indebted to the general practitioner for many of the outstanding advances in our science, and even if this were not so, the general practitioner is still in a position to evaluate the patient's complaints and physical findings and either treat the patient or intelligently refer him to one who can treat him better.

In my mind, the movement toward the narrower specialties may be directly traced to the fact that the general prac-

tioner has never been accorded his just professional recognition. To quote from an article by Dr Russell L Cecil in the May, 1945, issue of the *Medical Clinics of North America*: "during the last five decades a great variety of new specialties have appeared in the field, and many internists are devoting almost their entire time to such subjects as tuberculosis, diabetes, arthritis, allergic diseases and disorders of the endocrines. Personally, I believe this is a wholesome trend. However, it is very important for these highly specialized practitioners to maintain their contacts with the whole field of internal medicine. Otherwise, they become so narrow in their point of view that their approach to all medical problems is completely dwarfed. The rapid development of these subspecialties makes it difficult at times for the general practitioner to discover just what constitutes his domain today in the field of practice. Perhaps the establishment of group clinics will lead to a solution of these confused borderlines."

With a deep sense of respect and appreciation for all that Dr Cecil stands for in the world of medicine, I cannot but feel that this statement tends to put the general practitioner more or less out on a limb. In spite of this, he warns these highly specialized practitioners, the specialists, to keep close to general practice lest they become narrow.

What have our medical societies done for this large cooperative and all too submissive majority of medical men called general practitioners except to accept their support to further the exclusiveness of and to create more fellowships and boards for the minority specialists?

For the purpose of furthering the cause or elevating the status of the general practitioner, to me it seems needless to discuss his comparative mental equipment. Does it not require as much training, ability and experience to do well almost everything pertaining to the care of the sick as it does to do expertly just one division of this whole? It may be the opinion of many of our specialists that the general practitioner of tomorrow will be a kind of trained greeter or steerer whose chief function will be to find the groove in which his patient is put to get to the proper specialist. Contrary to this thought, numerous writings appear from time to time in reference to the lot of the general practitioner. Dr James L Halliday in the June, 1943, issue of the *British Journal of Medical Psychology* expressed the following opinion: "Members of our profession are becoming increasingly separated in function and the medical outlook of each is tending to be constricted to some partial or special view. As a result, there is a tendency to ignore the underlying system of medical thought which unifies our diverse observations and activities and enables us to place them in a proper setting and perspective." In this same article, Dr Halliday further states: "In the future of organized medicine, the general practitioner who has received a training in human biology will be pivotal in importance, and specialists will be regarded merely as his technical assistants."

Here and elsewhere, Dr Halliday has ably pointed out the fallacies into which a mechanistic concept of disease must lead. Sound etiology will force us to accept old Cicero's dictum, *Nisi humani alicuius a me puto*, which, freely translated, means "There isn't a thing about my patient that I may not need to know." No system of medical records no matter how skillfully contrived, can dispense with the integrating intelligence of a trained experienced mind. Here the sum of the parts is less than the whole. This integrating intelligence must stand near the beginning of the therapeutic process. There have been rhapsodies about the good old-fashioned family doctor. They are not all empty praise, although no doubt that good old fellow in the horse and buggy was paid half in cash and half in love, which was not the right formula. But we all know that the accomplishments of medical practice are not to be explained in engineering terms.

Now that I am no longer a general practitioner but have confined my work to internal medicine, I believe that it is not presumptuous of me to thus plead for recognition of the general practitioner. At the present time, any man who limits himself to a specialty, has, if qualified, an opportunity to pass the examination of a board and to become recognized by his fellows in his special field of work. This is true not only of the highly developed specialties, such as eye and x-ray, but also of the more comprehensive specialties, such as surgery and internal medicine. Why should not a well qualified general practitioner have the opportunity to pass a board examination in his general field that would put him

on equal footing with his brethren who have qualified in more limited fields?

With these thoughts in mind, why is it not feasible to establish the Board of General Practice or the American College of General Practitioners, or whatever it may be called, which would offer the same inducement to study and improvement that is accorded to men in other recognized specialties?

Those who have devoted years of study to the details of qualifications in the specialties would be abler than I to specify eligibility regarding training, hospital experience, practical experience and the amount, if any, of formal post-graduate instruction.

I am cognizant of the fact that the difficulties of setting up proper standards in such an inclusive specialty would be greater than those that have been experienced in the more limited fields. I am sure, however, this is not an unsurmountable barrier. Certainly it is worth the attempt, and such action would be a potent factor in raising the standards of and making more attractive the practice of general medicine.

Should my hopes and pleadings bear fruit, I am sure that the family physician, an American institution with more tradition and sentiment than any other branch of American medicine, will find a new life incentive and goal to work for and that this will bring righteous recognition from his fellows. His will be a chance, similar to that of his confreres in the specialties, for appreciation and recognition by the millions whom he serves day and night, regardless of the physical or mental troubles with which they may be afflicted.

FRED C ATKINSON, M D

257 Main Street  
North Andover, Massachusetts

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*The Examination of Reflexes. A simplification.* By Robert Wartenberg, M D. With a foreword by Foster Kennedy, M D. 12", cloth, 222 pp., with 7 illustrations. Chicago: The Year Book Publishers, Incorporated, 1945. \$2.50.

The author in this short manual has attempted to classify and unify the reflexes. Each reflex and the methods for testing and evaluation are discussed in a separate section. The important literature on the subject has been reviewed and noted in the text. A bibliography of 465 references is appended.

*The Management of Obstetric Difficulties.* By Paul Titus, M D, obstetrician and gynecologist, St. Margaret Memorial Hospital, Pittsburgh, and consulting obstetrician and gynecologist, Pittsburgh City Homes and Hospital, Mayview and Homestead Hospital, Homestead, Pennsylvania. Third edition. 8", cloth, 1000 pp., with 426 illustrations and 8 color plates. St. Louis: C V Mosby Company, 1945. \$10.00.

The first edition of this authoritative reference work was published in 1937, and the second in 1940, this third edition has been extensively revised to bring it up to date and incorporate the new material of the past five years. Additions and changes have been made in the chapters on sterility, ante-partum care, the general management of pregnancy, labor and the puerperium and their complications. X-ray pelvimetry has been rewritten and simplified, and the chapters on toxemia in pregnancy have been thoroughly revised, with the addition of a proposed new classification of toxemias. The chapter on intravenous infusions and blood transfusions has been completely revised, and the related subjects of Rh incompatibilities and erythroblastosis brought up to date. Caudal analgesia has been added to the chapter on anesthesia. The technique of extraperitoneal cesarean section are described, with a number of detailed new illustrations. The use of penicillin in puerperal sepsis, gonorrhea and syphilis complicating pregnancy, and in pyelitis and other infections, as well as the dosage and technique of administration, are discussed in considerable detail. This book should be in the reference libraries of obstetricians and all physicians practicing obstetrics, as well as medical libraries, especially those of hospitals.

*Courage and Devotion Beyond the Call of Duty Being a partial record of official citations to medical officers in the United States Armed Forces during World War II* Preliminary edition 16", paper, 254 pp Evansville, Indiana Mead Johnson and Company, 1944

In this preliminary edition, short sketches are provided of various physicians who have received military and naval awards for courageous action in combat or for outstanding achievement in medical service. Short biographies are listed alphabetically, and each describes briefly the action for which the citation or award was made. This small book is unusual and a worth-while addition to the medical history of World War II.

*Estudos Cirurgicos* Vol 4 Eurico Branco Ribeiro, director of Sanatorio Sao Lucas 8", cloth, 280 pp, illustrated Sao Paulo, Brazil Libreria Atheneu, José Bernades, 1945

In this volume Dr Ribeiro has continued his collection of clinical cases covering the whole field of surgery. A number of the interesting cases are documented with selected lists of references to the medical literature. A combined index for the four volumes of studies has been appended to the text, making available all the cases in the four series, the first of which was published in 1934.

*Penicillin Therapy, including Tyrothricin and Other Antibiotic Therapy* By John A. Kolmer, M.S., M.D., Dr P.H., Sc.D., LL.D., L.H.D., professor of medicine, School of Medicine and School of Dentistry, Temple University, and director of the Research Institute of Cutaneous Medicine 8", cloth, 302 pp, with 22 illustrations and 20 tables New York D. Appleton-Century Company, Incorporated, 1945 \$5.00

This small book has been written for the medical and dental professions and is largely based on the literature for 1944 and 1945. Various methods of administration are fully discussed. Necessary laboratory procedures are included.

## NOTICES

### ANNOUNCEMENTS

Dr R. Cannon Eley has returned from naval duty and will resume the practice of pediatrics at the Children's Hospital, 300 Longwood Avenue, Boston

Dr Benjamin Cohen announces his return from military service and the opening of an office for the practice of psychiatry and neurology at 520 Beacon Street, Boston

Dr James M. Faulkner, having returned from military service, is resuming the practice of internal medicine at 262 Beacon Street, Boston

Dr Calvin B. Faunce announces his return to the practice of otolaryngology at 290 Commonwealth Avenue, Boston

Dr Joseph Hahn, on termination of his military service, announces the reopening of his office at 121 Chestnut Street, Springfield

Dr Samuel Levine, having returned from military service, announces the opening of an office at 40 Baltimore Street, Lynn, for the practice of orthopedic surgery

Dr Henry M. Pollock, Jr., announces his separation from military service and the opening of offices for the practice of urology at 549 High Street, Westwood, and 536 Commonwealth Avenue, Boston

Dr N. S. Scarcello announces that he has been released from active duty with the United States Navy and will resume the practice of urology at 11 Irving Street, Worcester

Dr D. Thomas Staffier announces the removal of his office to 21 Breed Street, East Boston

Dr Jonathan Zonis announces the removal of his office from 300 Seaver Street, Roxbury, to 371 Commonwealth Avenue, Boston

## GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, April 9, at 8:15 p.m. Dr. Alvan L. Barach will speak on the subject "Treatment of Chronic Pulmonary and Sinus Infections." A discussion by Dr. Maurice S. Segal and Dr. Daniel Miller will follow.

## NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular annual meeting of the New England Dermatological Society will be held in the Skin Out-Patient Department of the Boston City Hospital on Wednesday, April 10, at 2:00 p.m.

## JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9-10 a.m.

### MEDICAL CONFERENCE PROGRAM

Wednesday, April 3 — Cerebral Hemorrhage Dr. R. D. Adams

Friday, April 5 — Experiences with the Use of Universal Donor Blood and Pooled Plasma Transfusions Dr. C. P. Emerson

Wednesday, April 10 — Medical Experiences in the Navy Dr. R. P. McCombs

Friday, April 12 — The Roentgenological Changes in the Gastrointestinal Tract in Scleroderma Dr. R. Scharzki

Wednesday, April 17 — The Diagnosis of Ruptured Membranes by the Vaginal Smear Dr. G. A. Bourgeois

Friday, April 19 — Holiday

Wednesday, April 24 — Atrophies, Hypertrophies, and Neoplasms of the Skin Dr. F. M. Thurmon

Friday, April 26 — Vagus Resection in the Management of Peptic Ulcer Dr. F. D. Moore

On Tuesday and Thursday mornings, Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek. Medical rounds are conducted by some of the staff members from 12:00 to 1:00 in the Lecture Hall.

All exercises are open to the medical profession.

## AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The general oral and pathological examinations (Part II) for all candidates will be conducted at Chicago, by the entire Board from Monday, May 6, through Saturday, May 11, 1946. The Palmer House in Chicago will be the headquarters for the Board. Formal notice of the exact time of each candidate's examination will be sent to him several weeks in advance of the examination dates. Hotel reservations may be made by writing direct to the Palmer House.

Candidates for re-examination in Part II must make written application to the secretary's office not later than April 15.

Candidates in military or naval service are requested to keep the secretary's office informed of any change of address. Deferment without time penalty, under a waiver of the published regulations applying to civilian candidates, will be granted if a candidate in service finds it impossible to proceed with the examinations of the Board. Applications are now being received for the 1947 examinations. For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, 6.

(Notices continued on page xix)

# The New England Journal of Medicine

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Volume 234

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Number 14

## THE PENETRATION OF PENICILLIN THROUGH NORMAL AND INFLAMED MENINGES\*

LIEUTENANT COLONEL J MURRAY KINSMAN, M C, A U S, AND

CAPTAIN C ANTHONY D'ALONZO, M C, A U S

**F**OLLOWING the demonstration that penicillin exhibits a remarkable antibacterial effect against organisms frequently causing meningitis, there immediately arose the question of the most effective mode of its administration in patients with these infections. Before penicillin was used in the treatment of meningitis, it was necessary to study its distribution in the body, particularly in the spinal fluid after extrathecal administration. Rammelkamp and Keefer<sup>1</sup> demonstrated that the meninges and the choroid plexus form a partial barrier against the passage of the drug from the blood stream into the spinal fluid, both in normal persons and in patients with meningitis. As a result of their investigations, it became the practice to give penicillin both extrathecally and intrathecally when it was used in purulent meningitis.

In general, the results with this combined form of therapy have been good.<sup>2,3</sup> Recently, however, McDermott, Eagle and Nelson<sup>4</sup> have shown that low concentrations—those of 0.02 units per cubic centimeter or less—of penicillin appear in the spinal fluid of normal persons several hours after massive parenteral doses. That inflamed meninges are more susceptible to the passage of penicillin than are normal ones was suggested by experiments in which constant amounts of the drug were injected intrathecally and assays of the blood and spinal fluid were performed at intervals thereafter. These studies showed that when the meninges are inflamed, the penicillin is absorbed from the spinal fluid more rapidly than it is in normal subjects.<sup>5</sup> Evidence tending to confirm these observations has been presented by Fleming<sup>6</sup> and more recently by Rosenberg and Sylvester.<sup>7</sup> The latter reported that they had found penicillin in the spinal fluid in patients with meningitis who had been treated by the intramuscular or the intravenous route alone. Price and Hodges<sup>8</sup> reported that 4 patients were cured, both clinically and bacteriologically, follow-

ing extrathecal therapy, 3 of them had meningococcal meningitis and 1 had pneumococcal meningitis. They mention 2 other patients in whom the cause of recovery was difficult to evaluate because they had received large doses of sulfonamides prior to penicillin therapy. In none of these cases were assays of the blood or spinal fluid performed. These observations have naturally suggested that intrathecal administration of penicillin is not necessary.

On the other hand, there is evidence that extrathecal therapy alone is sometimes inadequate. Some patients with pneumococcal pneumonia have developed pneumococcal meningitis while under treatment with penicillin administered by the intramuscular route.<sup>9</sup> Moreover, in a few patients with pneumococcal<sup>9</sup> and meningococcal<sup>10</sup> meningitis there was a poor response to penicillin therapy until it was given intrathecally.

Because of the conflicting reports, it seemed advisable to obtain further information concerning the most efficient mode of administration of penicillin in patients with meningitis, this was considered especially important because of the comparatively high incidence of meningitis in wartime. Studies have been conducted in this hospital concerning the penetration of penicillin into and out of the spinal fluid. The results of these studies, together with certain clinical observations concerning the effectiveness of extrathecally administered penicillin in the treatment of meningococcal meningitis, comprise the present report.

### ASSAY OF SPINAL FLUID FOLLOWING INTRATHECAL ADMINISTRATION

To determine how long penicillin persists in the spinal fluid after intrathecal administration, 4 patients with meningococcal meningitis were treated according to the following schedule: a dose of 25,000 units was given intravenously and one of 10,000 units intrathecally at the same time, one hour later, a dose of 25,000 units was given intramuscularly and repeated every three hours, the intrathecal injection was again administered at the

\*From the Medical Service Regional Station Hospital Fort Bragg, North Carolina.  
Part of this study was done under the direction of Lieutenant Colonel North C. Daniels, A. C., A. U. S.

eleventh hour Spinal fluid was collected for assay at the eighth and twenty-fourth hours. The specimens taken at the eighth hour contained 3.9 to 20.0 units per cubic centimeter, and those taken at the twenty-fourth hour contained 0.078 to 0.312 units. The penicillin content of the spinal fluid eight hours after the intrathecal injection of 10,000 units was thus shown to be far in excess of the minimum therapeutic requirement, and sixteen hours later, after a second intrathecal injection of 10,000 units, it was still at a therapeutically effective level. This indicates that when penicillin is used intrathecally for meningitis, it is not necessary to repeat the injections oftener than once every sixteen hours. Moreover, further observations in the same cases suggest that injection once every twenty-four hours is sufficient.

#### ASSAYS OF SPINAL FLUID FOLLOWING EXTRATHECAL ADMINISTRATION

##### *In Patients Without Meningitis*

More than 20 patients with early syphilis without meningitis were given intramuscular injections of 20,000 to 40,000 units of penicillin every three hours for one to eight days, and the spinal fluid was assayed at various intervals from the fifth to the eighth day. In no case was penicillin detected in the spinal fluid.

##### *In Patients with Meningococcemia*

Since it is now generally accepted that meningococcal meningitis is a sequel to or a metastatic form of a bacteremic phase, it was thought that in meningococcemia penicillin might possibly diffuse more readily into the spinal fluid than it does in normal persons. Specimens of the spinal fluid of 6 patients with meningococcemia who were being treated by penicillin were therefore collected for assay. Five of the patients received an initial dose of 25,000 units intravenously, which was repeated one hour later and then every three hours day and night. The spinal fluid was collected at the eighth and twenty-fourth hours of treatment in 4 cases and at the fifth and ninth days in 1 case. The sixth patient was on the same schedule, but in this case each dose was 40,000 units and the spinal fluid was collected at the eighth and twenty-fourth hours. In not one of the twelve specimens of spinal fluid was any penicillin detected, although in every case the clinical response to treatment was excellent and in no case did meningitis develop.

##### *In Patients with Meningitis*

**Tuberculous meningitis** Prior to making observations on patients with meningococcal meningitis, 2 patients with tuberculous meningitis were given penicillin by extrathecal injections and spinal fluid was obtained for assay. One patient was given five doses of 40,000 units each over a period of ten hours, the specimen of spinal fluid taken at the

eleventh hour contained a trace of penicillin, whereas that taken at the twenty-ninth hour contained none. The other patient received 40,000 units every three hours for eight doses, at the eighteenth hour no penicillin could be found in either the blood or the spinal fluid, whereas at the twenty-third hour the blood contained 0.4 units per cubic centimeter and the spinal fluid a trace of penicillin. In spite of large doses, therefore, only a trace of penicillin could be found in the spinal fluid after eleven hours of treatment in one case and after twenty-three hours of treatment in the other.

**Meningococcal meningitis** In view of the reported successes in treating meningococcal meningitis with penicillin administered only extrathecally, a study was made of the distribution of penicillin and its effectiveness in this disease when administered by the intramuscular route. Two case reports illustrating these points follow.

**CASE 1** A 33-year-old soldier was admitted to the hospital on November 18, 1944, at 3:40 p.m. At 8 a.m. of that day he had had a chill, and he later developed a splitting headache. On admission he showed fever, an erythematous rash, marked rigidity of the neck, bilateral Kernig and Brudzinski signs, absent knee jerks and drowsiness. The spinal fluid contained 1540 cells per cubic millimeter, gram-negative intracellular diplococci were found on the smear, and Group I meningococcus was obtained from the culture.

It was decided to treat the patient with penicillin by the extrathecal route alone. Accordingly, at 5:45 p.m. he was given 40,000 units intravenously (Fig. 1). One hour later

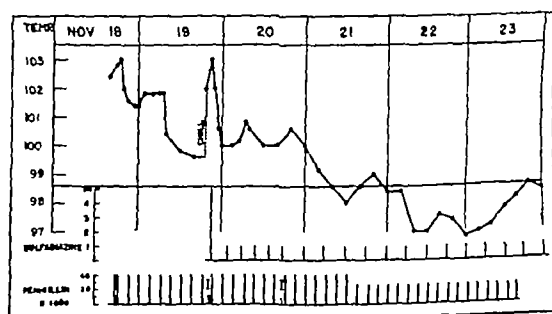


FIGURE 1 Case 1

This is the temperature curve of a patient with meningococcal meningitis who was treated initially only with penicillin. The dotted lines under 1 in the penicillin dosage zone represent intrathecal injections.

he received 40,000 units intramuscularly, and this dose was repeated every 3 hours. During the next 24 hours the temperature fell to 99.6°F, the rash disappeared, the Kernig sign became less pronounced, the knee jerks returned, and the patient became less lethargic and drowsy. The headache, however, appeared to be as severe as ever. The spinal-fluid cell count rose to 9000 by 8:45 a.m. on November 19 and dropped to 3450 at 5:45 p.m., and the pressure fell from 210 to 125 mm (Table 1). All specimens subsequently yielded meningococci on culture. At 7:20 p.m. on November 19, 25 hours after the first dose of penicillin, the patient had a sudden chill, and the temperature rose to 102°F and a half-hour later to 103°F. At the same time the headache became still severer, the rigidity of the neck increased, the Kernig sign became more pronounced, and the patient became more lethargic. The spinal fluid obtained 1 hour after the chill contained 6200 cells, almost twice as many as did the speci-

men taken 3 hours previously, and the pressure had risen from 125 to 285 mm. At 9 p.m. sulfadiazine therapy was instituted in addition to the penicillin, which was continued, and from this time on the patient made a rapid and complete recovery. Blood cultures taken throughout the course of the illness were negative.

*Comment* For a while this patient appeared to be responding to penicillin, although the improvement was less rapid than that usually produced by sulfadiazine. Taking into consideration the clinical relapse and the supporting

established by examination of the spinal fluid, which contained 4650 cells per cubic millimeter and in which gram-negative intracellular organisms were demonstrated on smear (Table 3).

Because it was possible to keep the patient under close observation, it was decided to begin therapy with penicillin alone. This was begun at 10 p.m. on January 22 with a dose of 40,000 units intravenously and 40,000 units intramuscularly, the latter being repeated at 11 p.m., midnight and 1 a.m. and every 3 hours thereafter. There was some

TABLE 1 *Spinal-Fluid Findings in a Case of Meningococcal Meningitis (Case 1)*

DATE	HOUR	PRESSURE	APPEARANCE	NO OF CELLS	POLYMORPHONUCLEAR CELLS	SMEAR	CULTURE
		mm			%		
11/18/44	5 20 p.m.	—	Cloudy	1 540	95	Meningococcus	Meningococcus Group I
11/19/44	1 45 a.m.	210	Cloudy	6 250	96	Negative	Negative
	8 45 a.m.	140	Cloudy	9,000	93	Negative	Meningococcus Group I
	5 45 p.m.	125	Cloudy	3 450	88	Negative	Meningococcus Group I
11/20/44	8 45 p.m.	285	Cloudy	6,200	88	Negative	Negative
	5 45 p.m.	110	Cloudy	4 300	87	Negative	Negative
11/23/44	10 00 a.m.	68	Clear	6	50	Negative	Negative

bacteriologic evidence, however, the case must be definitely classified as one of failure of penicillin to effect a cure. It is of interest that the only time a measurable level of penicillin was present in the spinal fluid was 27 hours after parenteral therapy was instituted, shortly before sulfadiazine was administered (see Table 2).

*CASE 2* An 18-year-old soldier was admitted on January 20, 1945. He apparently had a mild upper respiratory infection, and was about to be discharged on January 22 when

clinical improvement (Fig. 2) but not of a marked degree, and because the patient's condition remained poor, sulfadiazine therapy was begun on January 23, 20 hours after the first dose of penicillin. A little later the temperature rose to 103°F. Both sulfadiazine and penicillin were continued, and there was rapid and complete recovery. Blood cultures taken throughout the course were negative.

*Comment* As in Case 1, there was an initial improvement followed by a relapse and sulfadiazine was necessary for cure.

TABLE 2 *Assays of Blood and Spinal Fluid for Penicillin in 8 Patients with Meningococcal Meningitis Who Received Penicillin Extrathecally*

CASE NO.	DOSAGE OF PENICILLIN	INTERVAL BETWEEN INJECTION AND COLLECTION	PENICILLIN CONTENT	
			BLOOD units/cc	SPINAL FLUID units/cc
1	40 000 units intravenously 40 000 units intramuscularly 1 hr later and every 3 hr thereafter	hr		
		8	0.3125	0
		15	0	0
		24	0.3125	0
2	40 000 units intravenously and 40 000 units intramuscularly 40 000 units intramuscularly 1 2 and 3 hr later and every 3 hr thereafter	27	0.0195	0.04
		1 3/4	1.0	0
		2 3/4	0.5	0
		10	0	0
3	Same as in Case 2	16	0	0
		1 3/4	1.0	0.05
		2 3/4	1.0	0.04
4	Same as in Case 2	1 3/4	0.5	0
		2 3/4	0.5	0.05
5	Same as in Case 2	1 3/4	0.4	0
		2 3/4	0.5	0
6	Same as in Case 2	2 3/4	—	0.05
		2 3/4	—	0.05
7	25 000 units intramuscularly repeated 1 hr later 40 000 units intramuscularly 3 hr later and every 3 hr thereafter	22	—	0.05
8	40 000 units intramuscularly 100 000 units intravenously 1 hr later; 25 000 units intramuscularly 5 hr later and every 3 hr thereafter	35*	—	0*
9	30 000 units intravenously 100 000 units intravenously 3/4 hr later; 20 000 units intramuscularly 3 hr later	5†	—	Trace†

\*Patient died at 35th hour after the first injection. Spinal fluid was collected at autopsy 13 hours later.

†Patient died at 5th hour after the first injection. Spinal fluid was collected at autopsy 2 hours later.

he had a chill, followed by fever. He gradually developed a splitting headache, a sore throat and stiffness of the neck. Examination later in the day showed a fine macular eruption, moderate rigidity of the neck, positive Kernig and Brudzinski signs and sluggish reflexes. By this time the patient was semicomatose. A diagnosis of meningococcal meningitis was

In this case the relapse occurred 20 hours after the institution of penicillin therapy as compared with 25 hours in Case 1. No penicillin was found in the spinal fluid at any time (see Table 2). Throughout the period of penicillin therapy the cell count remained elevated and both smears and cultures were positive.

Following these experiences there was felt a natural reluctance to attempt to treat other patients with penicillin by the extrathecal route alone. Since, however, Rosenberg and Sylvester<sup>7</sup> had found penicillin in the spinal fluid in 8 patients at one and a half and two and a half hours after a single intramuscular injection of 40,000 units of penicillin, it was decided to attempt to confirm

3 cases (Cases 3, 4 and 5) of the 4 in which extremely large doses were given in the beginning

DISCUSSION

The studies reported herein indicate that although parenterally administered penicillin may penetrate into the spinal fluid in patients with meningitis, it does so irregularly and in relatively low concentrations. These observations do not confirm those of Rosenberg and Sylvester,<sup>7</sup> who found measurable spinal-fluid levels in all of 10 cases of meningitis, with some values as high as 0.35 units per cubic centimeter. The differences are undoubtedly due in part to the fact that the assays in the present study were done by a modification of the Rammelkamp<sup>11</sup> serial dilution test, whereas Rosenberg and Sylvester used a turbidimetric method. A detailed discussion of assay procedures is beyond the scope of this paper, but in general it may be said that owing to the variable factor of lysis of sensitive staphylococci by penicillin, the reliability of turbidimetric methods such as that employed by Rosenberg and Sylvester is open to serious question. The fact that certain of the values that they obtained — as high as 0.35 units per cc — are so much higher than those in the present study following much larger doses of penicillin and than those obtained in other laboratories<sup>4</sup> makes this explanation all the more probable.

The fact that the 2 patients in the present series who failed to respond to extrathecal therapy alone did not have measurable amounts of penicillin in the spinal fluid, except for a trace on one occasion, presumably indicates an inability of the penicillin

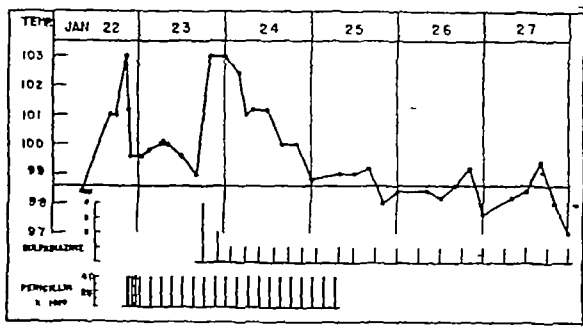


FIGURE 2 Case 2

This is another temperature curve of a patient with meningococcal meningitis who was treated initially only with penicillin

their results without jeopardizing the life of the patient by withholding other treatment. To be certain that a high concentration of penicillin was present in the blood stream, the doses used were large: at the outset a 40,000-unit dose was injected intravenously and the same dose intramuscularly. This dose was again given intramuscularly and 2 hours later. Specimens of blood and spinal fluid were collected for assay one and a half and two and a half hours after the beginning of treatment,

TABLE 3 Spinal-Fluid Findings in a Case of Meningococcal Meningitis (Case 2)

DATE	HOUR	APPEARANCE	NO OF CELLS	POLYMORPHONUCLEAR CELLS %	SMEAR	CULTURE
1/22/45	9 00 p m	Turbid	4 650	96	Meningococcus	Meningococcus Group I
	11 30 p m	Cloudy	8 300	93	Meningococcus	Meningococcus
1/23/45	12 30 a m	Cloudy	10 500	91	Meningococcus	Meningococcus
	8 00 a m	Cloudy	7 200	90	Meningococcus	Meningococcus
	2 00 p m	Cloudy	9 500	90	Meningococcus	Meningococcus

after which the patients were placed on sulfadiazine. The results in 4 cases (Cases 3, 4, 5 and 6) are recorded in Table 2, which also incorporates the results in the 2 cases reported above and in 3 cases (Cases 7, 8 and 9) in which assays were done at odd intervals. These studies showed that penicillin may indeed penetrate into the spinal fluid, although it does so irregularly and in low concentrations. Concentrations of the order reported by Rosenberg and Sylvester — that is, up to 0.35 units per cubic centimeter) — were not found in a single case, the highest level being 0.05 units. It should be emphasized that the blood levels were usually high — either 0.5 or 1.0 units per cubic centimeter — when measured at one and a half and two and a half hours after the beginning of treatment in

to penetrate readily into and through the meninges. This does not invalidate the favorable results obtained by Price and Hodges<sup>8</sup> from administration by the extrathecal route alone, but merely emphasizes the variability and irregularity in the appearance of therapeutic concentrations of penicillin in the spinal fluid when the drug is given in this manner.

The recent studies of Meads and his associates<sup>12</sup> reveal important information concerning a subject closely related to the problem of parenteral versus intrathecal therapy. It was found that certain strains of meningococci were relatively resistant to penicillin, some of them so much so that even with intrathecal and extrathecal penicillin therapy combined the results were not so good as those obtained

with sulfadiazine. These observations indicate that if penicillin is to be used in the treatment of meningitis, the concentration in the meninges and spinal fluid should be high enough to be effective against the relatively resistant organisms occasionally encountered. From the present studies, it is evident that when given only extrathecally penicillin penetrates into the spinal fluid too irregularly and in concentrations too small to satisfy fully these requirements. An exception to this is syphilitic meningitis, in which penicillin administered intramuscularly appears to give excellent results<sup>12, 14</sup>.

Four main points indicating that extrathecal therapy alone is not effective in meningitis have emerged from the present studies and from previous reports. These are the development of pneumococcal meningitis in patients receiving extrathecal penicillin therapy for pneumococcal pneumonia, the failure of many patients with pneumococcal and meningococcal meningitis to respond to penicillin until it was administered intrathecally, the low concentrations and irregularity of appearance of penicillin in the spinal fluid of patients with meningitis following extrathecal administration alone, and the fact that many cases of meningitis are caused by meningococci that are relatively resistant to penicillin.

It is therefore our opinion that patients with pneumococcal, streptococcal or staphylococcal meningitis should receive penicillin by both the extrathecal and intrathecal routes. For meningococcal meningitis, sulfadiazine is probably preferable to penicillin, but here too, if penicillin is administered, it should be given both extrathecally and intrathecally.

### SUMMARY AND CONCLUSIONS

Because of the conflicting evidence for and against the intrathecal versus the extrathecal administration of penicillin in the treatment of meningococcal meningitis, a study has been made concerning the penetration of this drug into and through the spinal fluid.

When doses of 10,000 units of penicillin were injected intrathecally in patients with meningococcal meningitis who were also receiving moderately large doses intramuscularly, therapeutically effective amounts were still present in the spinal fluid sixteen hours later.

In more than 20 patients without meningeal involvement who were given intramuscular injections of 10,000 to 25,000 units of penicillin every three hours, penicillin was not found in the spinal fluid in a single case after five to eight days of therapy.

In 5 patients with meningococcemia without meningitis who received 25,000 units of penicillin

intramuscularly every three hours, and in 1 who was given 40,000 units on the same schedule, penicillin was not found in the spinal fluid in any case after eight and twenty-four hours of therapy in 5 cases and after five and nine days in 1 case. Every patient recovered, and in no case did meningitis develop.

In 2 patients with tuberculous meningitis who were treated extrathecally alone, only a trace of penicillin could be found in the spinal fluid — after eleven hours of treatment in one case and after twenty-three hours of treatment in the other.

In 9 patients with meningococcal meningitis who were treated during the early part of their illness with penicillin extrathecally only, assays of the spinal fluid were performed at various time intervals after the beginning of therapy. In some cases no penicillin could be demonstrated in the spinal fluid at any time up to thirty-five hours, in others small amounts, never larger than 0.05 units per cubic centimeter, were found. The appearance of penicillin in the spinal fluid after large extrathecal doses was irregular and inconstant.

The case histories of 2 patients with meningococcal meningitis who were treated with comparatively large doses of penicillin extrathecally are presented. In each case relapse occurred after an initial period of improvement — after twenty hours of therapy in one case and after twenty-five hours of therapy in the other. Both patients promptly recovered under sulfadiazine therapy.

Penicillin penetrates the meningeal barrier too erratically to justify its use extrathecally alone in purulent meningitis.

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## CLOSURE OF COLOSTOMIES

## With Report of a Case

LIEUTENANT COLONEL PHILIP S FOISIE, M C, A U S \*

THE abdominal cavity, on account of its size and central location, offers a conspicuous target for pieces of flying shell fragments, so that it is not surprising that every trainload of recently wounded patients arriving at an Army general hospital includes a fair number with abdominal injuries. Those that we have received were in fair condition on admission. In a few cases, the wound had been closed when exploration revealed no perforation of the bowel. In some, large hematomas had been found or other nonintestinal injuries had been repaired, but in the largest group of cases there was a history of bowel perforation, often multiple. In most of these, wounds of the small bowel had been sutured or resections had been done when the trauma was extensive. Many of these patients had primary closure with good results. In most cases of injury to the large bowel, the injured site had been exteriorized; and most cases that presented any great amount of bowel damage had received colostomy. Only in occasional cases did the record state that the limbs of bowel had been sutured together to form a well defined spur. By digital examination, however, it was possible to decide which cases were suitable for crushing, and most of the cases were prepared for closure in this manner. In 26 cases, colostomies were closed by applying clamps to reduce the septum between the bowel loops, and this was followed by simple transverse suture of the stoma, after the bowel had been freed to below the peritoneum and the adjacent rim of skin, with any protruding and edematous portion of the bowel, had been resected. It was usually found that this section of the bowel was fairly well walled off from the general peritoneal cavity by intraperitoneal adhesions, and no attempt was made to free them. After closure the bowel was dropped into the abdominal cavity and the peritoneum was closed over it, but the adhesions were not completely freed in the general peritoneal cavity. These patients had extremely little post-operative reaction or distention. Such a procedure can be carried out through a small elliptical incision, a small margin of skin around the stoma being excised, even when it is situated well in the flank or close to the inguinal region.

In only 2 cases were the loops resected and the free ends anastomosed. In one of these, a large mass of bowel had been exteriorized onto the abdominal wall following extensive injury to the descending colon. In the other case, a large amount of protruding bowel was eroded and thickened from exposure and was so situated laterally as to offer

little opportunity for freeing it up in situ. In this case the bowel was closed externally, covered with a rubber glove and brought back into the abdomen, and after resection of the entire mass a lateral anastomosis done.

Whether the limbs of bowel are sutured together to form a spur suitable for subsequent crushing or a loop of bowel is brought to the surface with no attempt to approximate its limbs, a certain amount of spur is bound to result. Efferent and afferent limbs adhere to some extent by their approximation in passing through the abdominal wall. All that is necessary to allow room enough for subsequent closure is to crush a portion of the intervening septum. Almost any type of surgical forceps is satisfactory for this purpose. The Kelly forceps suffices when only a small bite needs to be taken, but it is rarely comfortable to close the instrument to the first notch when it is first applied, and since it has no tooth at the tip, it is likely to slip off as the edema subsides. The Ochsner forceps overcomes this disadvantage but takes an extremely small bite. We generally use a pylorus clamp for the first application, employing the Kelly forceps later if a little more of the septum must be taken. The instrument is closed only to the point where it begins to be uncomfortable, and the bite is held with a strip of adhesive tape around the handles of the forceps. The slack can be taken up gradually every two or three hours with new strips as edema subsides until the first notch is reached. It is not necessary to apply two parallel clamps and slough out the central section. As soon as a cut is made in the septum it separates, and this forms an adequate lumen.

A practical criterion as to the adequacy of the preparation is the patient's ability to resume normal bowel movements. Patients admitted with evacuation occurring exclusively through the abdominal stoma begin to have normal defecations after some of the opposed bowel wall has been crushed. We have frequently tested this function by plugging the stoma with a vaseline gauze pack supported by a firm pressure dressing. This serves to encourage normal defecation if the lumen is adequate and also reduces any herniation of the bowel, as well as any edema in the exposed portion. Occasionally this results in complete reduction of the bowel beneath the skin margin and almost complete spontaneous closure. We have not waited for this to occur, however, since it still leaves bowel tied into the abdominal wall and requires unnecessary time. In such cases it is necessary only to excise the skin margin and close the small remaining opening into the bowel with a purse-string suture.

\*Instructor in surgery, Tufts College Medical School and assistant to visiting surgeons, Boston City Hospital (on leave of absence)

The bowel can then be freed from the abdominal wall, the peritoneum closed over it, and the defect in the abdominal wall repaired. The wound is closed without drainage.

In some circumstances there is some question whether sufficient lumen has been left after closure

on the amount of lumen present. This is particularly true when the absence of a well defined spur has made it advisable to do little or no crushing. In such cases a transverse closure is done, and if it is thought that this has resulted in a questionably small lumen at the point of closure, an auxiliary

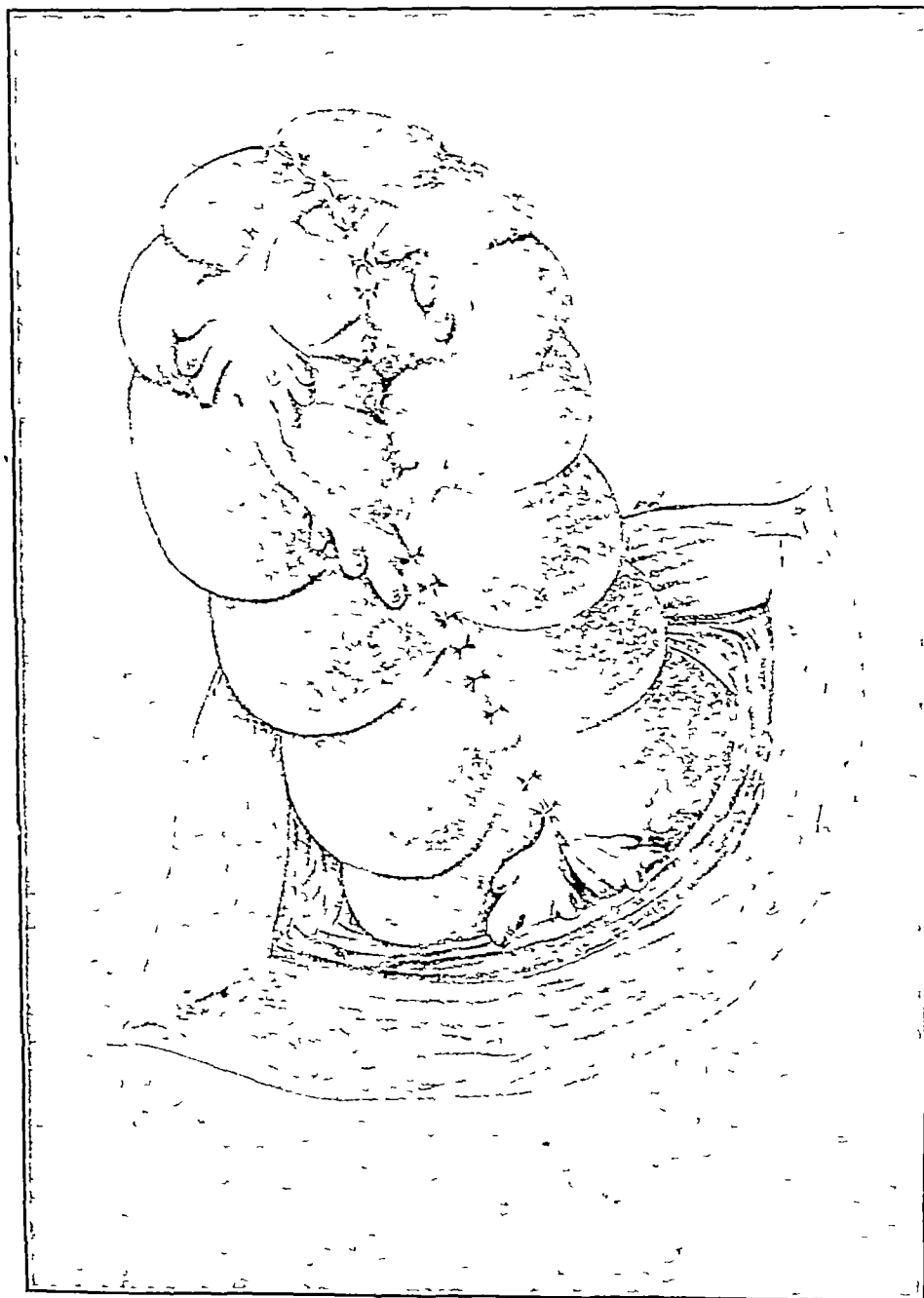


FIGURE 1 Completed Closure by Transverse Suture at the Site of Colostomy, with Anastomosis of Adjacent Loops in Cases in Which the Closure Leaves a Lumen of Questionable Adequacy

of the bowel. This happens when the opening is particularly large so that its inversion with two layers of sutures may have encroached too much

stoma is made by a lateral anastomosis of the adjacent limbs as they lie side by side in the portion of the bowel that traverses the abdominal wall

(Fig 1) This is done through the smooth longitudinal band of the antimesenteric margin, which can be easily approximated, since these loops of bowel are usually found bound together by adhesions incident to their displacement into the abdominal wall. In this way a satisfactory intestinal stream is re-established without sacrificing any blood supply to the bowel and without breaking through the protective walling-off process that to some extent at least seals off the local area of affected bowel from the general peritoneal cavity. Apart from the safety factor that this more conservative procedure affords, the postoperative course is milder than it is in cases in which resection and anastomosis are done.

#### PREOPERATIVE PREPARATION

As soon as colostomy patients are admitted, the record is studied to learn the extent and nature of the original bowel injury and to ascertain what was done at the forward hospital. A digital examination of the stoma is then made to determine whether the loops lie in close approximation and to gauge the thickness of the intervening septum. If the loops diverge immediately and there is a bulk of intervening tissue, no crushing is attempted. In most cases the two loops are found to lie parallel for several centimeters, with only a thin septum consisting of the two bowel walls, so that there is ample opportunity for crushing between them, even when the record makes no mention of the formation of a well defined spur. Clamps are applied as described above, several small bites being taken in preference to including too much tissue in the first application. The clamps usually fall off in three days, and a day or two more is allowed for any edema to subside before making a reapplication, if this is considered necessary. As a result of blood loss incident to the original injury and the emergency operative procedure, and because of the somewhat impaired nutrition secondary to the altered bowel habits, the blood picture in most of these cases is somewhat below normal. From one to three transfusions have been required to restore a normal circulation before any type of closure is done. There is a week of preoperative preparation after the patient appears to be anatomically ready for closure. During this period the proximal and distal loops are irrigated daily with warm saline solution and an occasional enema is given. Since no succinylsulfathiazole is available in this area, 1 gm of sulfaguanidine is administered every four hours during the week of preparation. A low-residue diet is given beginning four days prior to operation, and during the final twenty-four hours only clear fluids are given. Multi-vitamin preparations are given from admission until the patient has regained ability to tolerate a full diet postoperatively. A thorough cleansing of both loops of the colostomy is done on the evening before operation and again

just prior to leaving the ward for the operating room.

#### POSTOPERATIVE CARE

On the patient's return from the operating room the following routine is employed. A transfusion of 500 cc of whole blood is given immediately and is repeated if indicated. Drainage with a Wangenstein tube is done until flatus is being passed spontaneously and the abdomen is perfectly soft, this period averages three days. A dose of 3000 cc of 5 per cent glucose in normal saline solution is given daily until the patient begins to take fluids, and in some cases 1000 cc is given daily for one or two more days. Penicillin is administered, 40,000 units being included in each infusion.

The patient receives 16 mg of morphine every four hours for the first day and as needed thereafter. On about the third day the suction tube is clamped.



FIGURE 2 *An Abdominal Wound Caused by a Shell Fragment. The suture line of the exploratory incision has separated. There is a large defect in the lower abdominal wall opening directly into the abdominal cavity. A clamp has been applied to the colostomy spur. Note the extensive denuded area. Evacuation of the entire bowel drainage onto, and in fact into, this wound posed a difficult surgical and nursing problem.*

and the ingestion of small amounts of fluids by mouth is begun. If these are well tolerated, they are increased, and the patient is given a light diet for two days and then placed on a regular diet. There is usually normal defecation on the fourth day without an enema, and from then on convalescence is generally uneventful.

#### RESULTS

In this series of 26 cases, closure failed in only 1. In this case a small localized abscess was encountered alongside the bowel and deep in the abdominal wall.

In the face of this fact, no further freeing of the bowel was done, but it was closed in the hope of eliminating the fecal drainage as an aid to clearing up the infection. Drains of course had to be inserted into the abscess cavity. This closure broke down and fecal drainage persisted, and it took several weeks to clear up the infection in the abdominal wall. The patient finally had to be

subsequent paper on intestinal obstruction following abdominal wounds with bowel injury.

In 23 cases there were no complications. All these patients ran an extremely mild postoperative course and immediately developed normal bowel habits. They gained in weight and made general improvement, and were returned to the Zone of Interior in excellent physical and mental condition.

The case history of a patient with extensive abdominal trauma illustrates some of the many problems involved in the management of these cases.

A 35-year-old private was wounded on December 21, 1944, by a shell fragment which tore a large hole in the left lower quadrant of the abdominal wall. There had been evisceration of the ileum and jejunum with perforation of the jejunum and of the sigmoid colon. He had of course, experienced severe shock. On December 21 the jejunum was closed and the sigmoid exteriorized, and an unsuccessful attempt was made to close the abdominal wall.

The patient was evacuated to the United Kingdom on December 29, and was admitted to this hospital on January 2, 1945. The abdomen showed extensive loss of tissue (Fig 2). The operative incision had completely broken open

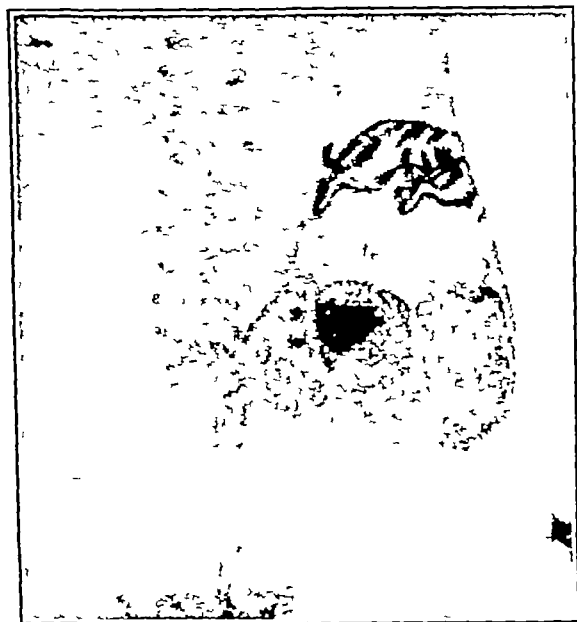


FIGURE 3 Photograph of the Same Abdomen at an Intermediate Stage

The midline wound has healed. The spur has been cut through, ready for closure of the bowel. There is still a large denuded area, which could not be grafted because of continual soiling. At this point, the patient was operated on, the colostomy was closed, the abdominal wall was repaired, and the skin defect was covered with split-thickness grafts.

evacuated with a persistent fecal fistula, but he was afebrile and had no further suppuration and had normal bowel movements as well. Final closure will have to be postponed until all inflammatory reaction has subsided. The patient was, however, gaining weight and doing well generally when evacuated to the Zone of Interior.

In 2 cases the wounds broke down slightly, with a small amount of fecal drainage for a few days. These wounds closed spontaneously, and there were no signs of peritoneal soiling.

There was 1 death in this series. It was caused by intestinal obstruction with massive gangrene of the bowel owing to adhesions resulting from the original trauma. The colostomy closure was functioning perfectly and was unrelated to the obstruction, which involved practically the entire small bowel, the latter being caught in multiple dense adhesions. This case will be discussed fully in a



FIGURE 4 The Final Result

The entire wound healed solidly, and normal bowel habits were restored. Note the skin grafts closing the defect seen in the previous illustrations.

and was held only by deep stay sutures. The bowel could be seen moving beneath the incision with respiration. Abdominal fluid welled up freely through the wound. A dark triangular area just medial to the colostomy opened into the abdomen and was constantly filled with feces. An area over the left iliac crest was completely denuded of skin, and the whole wound exuded with pus and feces.

The wound was strapped together with wide fenestrated strips of adhesive and was flushed several times a day, after the abdominal cavity had been protected as much as possible with wide strips of vaseline gauze. Cutting of the spur was begun at once (Fig 2). Several transfusions were given to build up the patient's general condition, and on January 9, under Sodium Pentothal anesthesia on the ward, a simple purse-string suture was applied to the colostomy in an at-

tempt to stop the fecal contamination of the open wound. This suture broke down in a few days. On January 17, a large abscess of the right thigh was drained. On January 30, pinch grafts were applied, and these stimulated the growth of points of epithelium that helped to close the wound. On February 24, a clamp was reapplied to cut the spur down a little more, and on March 5 preparation of the patient for closure of the colostomy was begun. There was still a large granulating area about the colostomy (Fig 3), but an adequate lumen had been established. On March 12, under spinal anesthesia, the bowel was freed and closed by a transverse suture. It was possible to close the peritoneum over the sutured bowel without completely freeing the intra-abdominal adhesions. There was some difficulty in repairing the defect in the abdominal wall owing to loss of fascia, but a flap of the external oblique muscle was used to close the wound securely. Split-thickness skin grafts were then applied, all the denuded areas on both sides of the colostomy being included.

The patient did extremely well. There was a small amount of leakage, which closed spontaneously, and the wound healed solidly (Fig 4). The patient developed normal bowel habits and gained in weight, and was returned home in excellent condition.

## SUMMARY

The closure of colostomies in 26 cases following battle injuries is reviewed. Most of these were closed without resection and without completely freeing the bowel. In cases in which the local closure resulted in a lumen of questionable adequacy, an auxiliary stoma was made in adjacent loops. Thus, a satisfactory bowel continuity was re-established with a minimal sacrifice of blood supply and with a mild postoperative course.

In this series a fair amount of intraperitoneal walling-off has been encountered. The re-establishment of adequate bowel continuity and closure without disruption of this protective mechanism seemed to minimize the severity of the postoperative course and to offer some protection against leakage and soiling.

An interesting and difficult case is presented.

## A NEW ANTISEPTIC SOLUTION FOR TOPICAL APPLICATION

### Comparative In Vitro Studies

ETHAN ALLAN BROWN, M R C S (LONDON), L R C P (ENGLAND),\* WILFRED KRABEK, M Sc,  
AND RITA SKIFFINGTON, B Sc

BOSTON

THE earliest written records contain references to the use of germicidal agents.<sup>1</sup> The standard drug encyclopedias<sup>2</sup> list more than one hundred official and nonofficial preparations used for this purpose. The voluminous literature concerned with antiseptics attests to the intense study that has been given this subject, one of paramount importance in the field of medicine.

The ideal antiseptic for topical application must be stable, nontoxic, nonirritating and nonallergenic. It must act fairly quickly, yet its action in mixed infections must be relatively long lasting and effective. Its properties should permit its safe application to tissues as different as are the skin and mucous membranes, as well as to the highly specialized epitheliums of the eye and ear and, perhaps, of the genitalia. There must be no esthetic objections to its color, odor or other physical characteristics. Other considerations, such as availability and price, are secondary but nevertheless important factors.

With this and other points in mind, almost all available antiseptic solutions were studied and classified, but each was found wanting in one or more of the necessary qualifications. A review of the history of topical antiseptics reveals that one of the oldest of present-day solutions, hydrogen peroxide, possesses the greatest number of the above-

listed advantages. Not only are its constituent and end products innocuous, but it is intimately related to bacterial metabolism.<sup>3</sup> It has fallen into disfavor because it suffers from two apparently major disadvantages: it is not stable in vitro, and its action in vivo is too transient to affect bacteria. The stabilization of hydrogen peroxide and the control of its rate of decomposition in catalase or peroxidase systems would open a new field in both peroxide chemistry and wound antiseptics.

It occurred to us that these problems could be solved by the use of carbamide peroxide as a solute and a source of hydrogen peroxide and that of anhydrous glycerol as a solvent. With the discovery that carbamide peroxide can be stabilized in alcohols and especially glycerol,<sup>4</sup> it seems that such solutions may have unusual antiseptic properties.

Studies of the action of 4 per cent carbamide peroxide in glycerol on fusiform bacteria<sup>5</sup> have shown that, by the agar-cup plate method, zones of inhibition are produced whose radial measurements from the edge of the cup to the edge of the zone are approximately 18 mm. A 0.125 per cent solution gives a zone of 5 mm. The glycerol control and the materials used for comparison—phenol (1 per cent), Pepsodent (undiluted) and Listerine (undiluted)—showed no zones of inhibition.

Further studies<sup>6</sup> demonstrated that following the oral use of carbamide peroxide solution (2 per cent in 50 per cent glycerol and 50 per cent water),

\*Instructor in medicine, Tufts College Medical School; consultant in allergy, Joseph H. Pratt Diagnostic Hospital; physician-in-chief, Allergy Clinic, Boston Dispensary.

the total number of viable bacteria in the oral cavity was reduced by 26 to 93 per cent for a period of two hours. The viable fusiform bacteria were reduced by 52 to 93 per cent. The number of bacteria, both viable and nonviable, were reduced by 10 to 62 per cent.

The use of this solution in 35 cases of chronic purulent otitis media<sup>7</sup> gave the following results. Three patients showed no improvement, and 3 required additional treatment. The condition cleared completely in 29 cases within four to thirty-eight days, and in 17 cases within fourteen days. Equally encouraging results were achieved in the treatment of infections of the skin, eyes and mouth and in varicose and diabetic ulcers. These results will be reported in later articles. In all, the solution has been used by more than thirty physicians on more than 650 patients, in studies extending over a period of four years. The present paper, part of an extended series on antiseptics, is concerned with laboratory data, the solution being compared with a number of standard preparations for a series of organisms generally present in infections of the skin and mucous membranes.

The solution consists of 4 per cent carbamide peroxide in substantially anhydrous glycerol. Experiments with an 8 per cent solution are included, although its use in patients was followed on several occasions by slight transient irritation. For purposes of identification, the solution has been tentatively named Thenardol, in order that it may commemorate Jacques Louis Thénard (1777-1855), the discoverer of hydrogen peroxide.

On contact with water, the carbamide peroxide is split into carbamide (urea) and hydrogen peroxide. The presence of catalase or peroxidase in the tissues causes decomposition of the hydrogen peroxide into water and oxygen. In the concentrations present, none of the contained substances are toxic, irritating or allergenic.

The uses of urea as a peptizing agent are too well known to require listing.<sup>8,9</sup> It should be noted at this point that all the previous studies concerning urea have dealt with its aqueous solution. Preliminary studies indicate that with the glycerol solution there is little or no absorption from wide areas of denuded tissues and no rise in nonprotein nitrogen.

The literature concerned with the antiseptic effects of hydrogen peroxide covers a period of more than sixty years, the greater part of it is unfavorable.<sup>10</sup> Many of the authors who have worked in this field have noted that its relative ineffectiveness is chiefly due to its rapid decomposition and therefore transient action in aqueous solutions. None of this literature is pertinent, since little previous work has been reported regarding the action of hydrogen peroxide in glycerol, in which the rate of decomposition is relatively slow. Noteworthy work has been done by Melenev,<sup>11</sup> who since 1935

has worked with slow-acting peroxides, especially zinc peroxide, in watery suspensions, and by Reid and Altemeier,<sup>12</sup> who used the same peroxide in ointment form. The latter investigators state that the organic peroxides tend to be unstable but that urea peroxide in ointment form, if carefully made, remains stable. No details of the process of preparing the ointment are given. Our technic of preparation gives us an organic peroxide in stable liquid systems.<sup>4</sup>

The biochemistry of glycerol has been reviewed in detail.<sup>13</sup> It has been stated<sup>14</sup> that it is used more frequently in prescriptions than is any other substance except water. The ingestion of 30 cc three times daily for fifty days by 14 normal adults was found to be harmless.<sup>15</sup> It should be noted that the absorption of glycerol, a factor to be considered in its application to large denuded areas, especially in diabetic patients, leads to the formation of glucose and glycogen.<sup>16</sup>

Although experimental work with wounds in animals<sup>17</sup> has shown that glycerol holds granulations in check and permits epithelium to advance, not all authorities agree that this is clinically true. Glycerol solutions are said to cause irritation, owing in most cases to their dehydrating properties.

The term "irritation" requires definition so as to make it clear whether it refers to the subjective feelings of the patient or to the objective observations of the investigator. It is also necessary to consider the length of time the antiseptic solution has been used and the type of lesion to which it has been applied. Almost all substances, including water, retard healing if left in contact with damaged tissue for a sufficiently long time.

In 4 of our patients, there were complaints of a burning sensation but no objective changes could be seen. In another patient, no irritative effects were noted until the solution had been used as a continuous wet dressing on an infected anterior abdominal wall for fifty days.

It appears from preliminary clinical studies that glycerol solutions, although irritating at the point in the patient's progress at which the infection is under control and exudate is at its minimum, are less irritant than are any of the antiseptic tinctures that the physician is likely to use, either prophylactically or therapeutically, for the same type of lesion at the same time. Irritation is of concern only when it occurs before the infection has been checked. When it does so at a later date, it merely gives warning that the antiseptic should have been discontinued, however difficult it is to choose the moment at which this should be done.

In the present solution, the hygroscopic property of the glycerol constitutes a valuable adjunct to the chemotherapeutic process, since it draws plasma from the deeper parts of wounds, thereby washing out micro-organisms and exposing them to antiseptic action. Its viscosity gives it the mechanical

advantage of both the liquid and ointment types of medication. One of the special virtues of the solution is that it does not dry when used as a wet dressing in chronic infections.

Our studies were concerned with more than one hundred antiseptic solutions, of which the following six, used for comparison, were chosen for the present paper: tincture of iodine (U S P), Tincture of Mercresin (standard strength), Mercurochrome (2 per cent aqueous), Tincture Metaphen (1 200),

of a twenty-two-hour to twenty-six hour dextrose broth culture of the organism to be studied and poured into a 90-mm petri dish with an unglazed porous top. After the agar had hardened, a 1.5-cm cup was cut with a sterile cork borer, and a drop of melted agar was introduced into the cup to fill any cracks present. With a sterile pipette, 0.2 cc of the antiseptic to be studied was placed at the bottom of the cup. Replicate experiments were performed three or more times for each solution.

TABLE 1 Measurement of Antiseptic Potency by a Modified Agar-Cup Plate Method \*

ORGANISM	ANTISEPTIC							
	TINCTURE OF IODINE (U S P)	THENARDOL (8%)	THENARDOL (4%)	TINCTURE METAPHEN (1 200)	TINCTURE OF MERCRESIN (standard strength)	MERCUROCHROME 2% (aqueous)	ZEPHIRAN CHLORIDE TINCTURE (1 1000)	TINCTURE OF PHEMEROL (1 1000)
A <i>Staph aureus</i> (FDA Strain 209)	19	19	18	(16)	(19)	(9)	11	9
B <i>Staph aureus</i> (lab strain)	20	17	12	(11)	(19)	(7)	10	(7)
C <i>Streptococcus</i> (alpha hemolytic)	28	22	20	11	(15)	6	8	10
D <i>Streptococcus</i> (beta hemolytic)	13	18	16	13	(15)	(6)	2	(3)
E <i>Enterococcus</i>	18	18	15	22	11	(3)	6	(3)
F <i>M epidermidis</i>	22	17	11	9	12	6	(8)	8
G Diphtheroid	22	24	(18)	11	(16)	6	(16)	5
H <i>P mirabilis</i>	13	17	16	(11)	(9)	(5)	(1)	(1)
I <i>Ps pyocyaneus</i>	21	16	15	(12)	(12)	(6)	4	(5)
J <i>Esch coli</i>	9	11	10	(13)	9	(6)	(1)	(1)
K <i>A aerogenes</i>	23	12	12	9	11	5	6	(2)
L <i>E typhosa</i>	24	16	14	25		5	(2)	(2)

\*The measurements are given in millimeters from the edge of the cup to the edge of the zone. The numbers in parentheses refer to the zones that gave positive subcultures and imply that the antiseptic solution at the point of subculture was bacteriostatic but not bactericidal.

Tincture of Phemerol (1 1000) and Zephiran Chloride Tincture (1 1000). The list includes a halogen, two mercurials, a mercury-phenolic compound and cationic agents dispensed as tinctures and as aqueous and glycerol solutions.

We appreciate the fact that 2 per cent aqueous Mercurochrome is not the vehicle in which the substance is said to show its greatest effects. Since it and the other solutions listed have been the subjects of study in all the forms in which they are available and will be reported in detail separately, mercurochrome was chosen as representative of an aqueous mercurial widely used for its supposedly antiseptic action.

These studies were concerned with the effects of antiseptic solutions on approximately forty pathogenic organisms, of which the following twelve are covered in this report: *Staphylococcus aureus* (FDA, Strain 209, and our own laboratory strain), alpha-hemolytic and beta-hemolytic streptococci, an enterococcus, *Micrococcus epidermidis*, a diphtheroid, *Proteus mirabilis*, *Pseudomonas pyocyaneus*, *Escherichia coli*, *Aerobacter aerogenes*, and *Eberthella typhosa*. The first seven organisms are gram-positive, and the remaining five are gram-negative.

The testing method used was a modification of the FDA agar-cup plate technic.<sup>18</sup> Bacto dextrose agar, 35 cc (pH 7.3), was inoculated with 0.2 cc

and for each strain. The results were consistent within significant limits.

The plate was immediately incubated at 37°C and read after eighteen hours. Approximately 0.25 sq cm of the medium was removed for subculture, being taken at a point 2 to 5 mm in from the edge of the clear zone.

Dextrose agar was chosen as the medium so that maximum growth might be achieved for the greatest number of species with uniform conditions for all. Brewer's thioglycollate medium was chosen for the subcultures, since it detoxifies the mercurials and counteracts any residual peroxide. It seemed to have little or no effect on the cationic solutions, such as Zephiran. Considering the number of subcultures necessitated by this work and the relatively small zones obtained under the conditions of the experiments, the use of cationic detoxicants of the type mentioned by Valko and DuBois<sup>19</sup> was not considered feasible.

The clear zone was measured radially in millimeters from the outside edge of the cup to the edge of the clear zone. When the zones were irregular in outline, five representative measurements were taken and an average figure was determined. When the zone edges were hazy, the exact zone was determined by subcultures taken

from the center of the plate toward the periphery The results are listed in Table 1

We are fully cognizant of the fallacies inherent in the conclusions that can be drawn from the type of test described These have been ably discussed by Nve,<sup>20</sup> many of whose suggestions have

and 4 per cent Thenardol The letters below the columns identify the organisms, according to the listing in Table 1 The negative sign (—) over a solid column evidences a negative subculture 2 to 5 mm central to the edge of the zone and implies that the column represents the zone of bac-

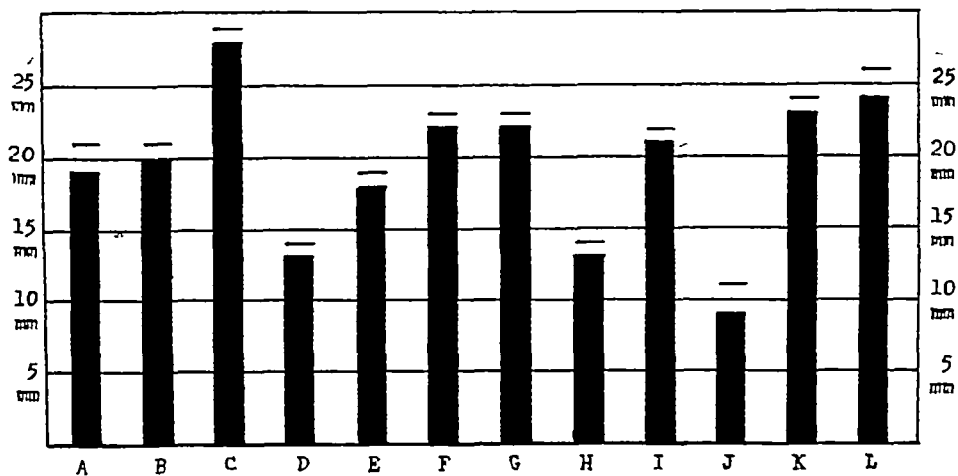


FIGURE 1 The Measurement of the Effects of Tincture of Iodine (U S P) on Twelve Common Organisms

been taken into consideration in this and the subsequent papers of the present series The test is, however, a standard one It does not control the effects of sublimation and so-called "creeping" for tincture of iodine and of creeping alone for other tinctures The inhibitions produced by such solutions therefore suggest greater effectiveness than do exact measurements of actual bactericidal action, thus showing them to their greatest advantage

tericidal power An open column indicates that subcultures were positive and implies that the antiseptic was bacteriostatic rather than bactericidal Subsequent reports will deal with the exact limitation of such zones of bacteriostasis, subcultures being taken radially at 2-mm intervals from the edge of the cup to the edge of the clear zone

It will be seen from the tables that tincture of iodine gives the largest zones As noted above

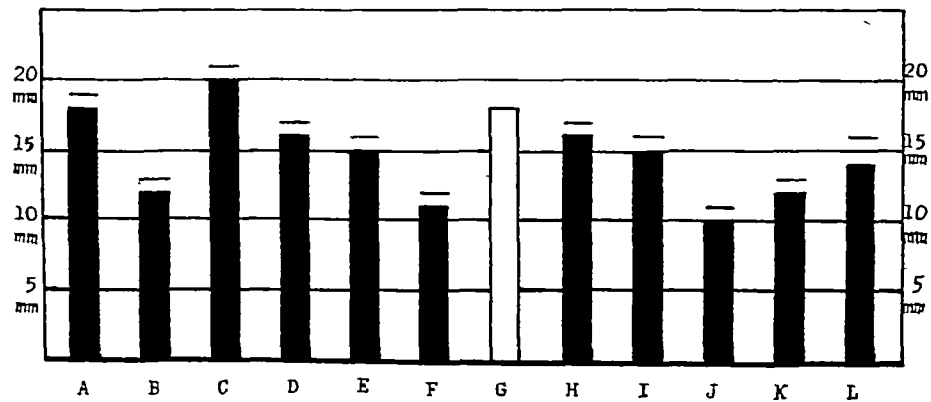


FIGURE 2 The Measurement of the Effects of Thenardol (4 per cent) on Twelve Common Organisms

The control of these qualities results in zones greatly reduced in size Since this work has not become generally known the traditional method has been used for the present paper

The accompanying charts (Figs 1 and 2) demonstrate the results for tincture iodine (U S P)

with correction for the effects of sublimation and creeping these zone are reduced in size by 2 to 20 mm The factors involved are varied and complex and require separate studies This fact holds equally true for the other tinctures, although to a lesser extent



The differences in effect on the members of the gram-positive (A-G) and the gram-negative (H-L) groups by the antiseptic solutions, especially the cationic detergents, as shown in Table 1, is worth noting. The antiseptics have been arranged in the approximate order of potency, as measured by the agar-cup plate method. As noted above, the measurements were taken radially from the edge of the cup to the edge of the zone in millimeters. Whenever subculture material was positive, the zone was considered one of bacteriostasis. In this event the measurements are enclosed in parentheses. Otherwise, the measurements refer to zones of bactericidal effect as proved by negative subcultures.

Since replicate experiments showed the behavior of the antiseptic solutions to be consistent for each organism, the inconsistent effects of differing organisms should be noted. Tincture of iodine and 8 per cent Thenardol demonstrated excellent bactericidal power. With 4 per cent Thenardol there were positive subcultures for the diphtheroid group. Tincture Metaphen appeared to be bacteriostatic for the staphylococci used and, in the gram-negative group, for *P. mirabilis*, *Ps. pyocyaneus* and *Esch. coli*. Tincture of Mercresin was bacteriostatic for seven of the bacteria, the subcultures being negative for the enterococcus, *M. epidermidis*, *Esch. coli* and *A. aerogenes*. For technical reasons, the results for *E. typhosa* have been omitted, the zone having been too irregular to be read with accuracy. Mercurochrome gave small zones for all the organisms, with positive subcultures for seven. Its effects were apparently less uneven than those of the other solutions studied. The action of Zephiran Chloride Tincture was extremely irregular, with little or no demonstrable effect on *P. vulgaris*, *Esch. coli* and *E. typhosa*. Tincture of Phemerol showed almost no bactericidal power for nine of the twelve bacteria. It affected the standard staphylococcus but not the laboratory strain, a much more resistant organism.

If tincture of iodine is taken as a standard, the great difference between its bactericidal power and those of the other solutions studied is quite remarkable and should do much to outweigh its irritant, toxic and allergenic properties, especially since the mercurials are themselves not free of these same faults. The agar-cup plate technic therefore appears to corroborate the previous studies, especially those of Nye,<sup>20</sup> who reached the same conclusions although using other technics in the evaluation of iodine

solutions. Since iodine cannot, however, be used either for applications at frequent intervals or for continuous wet dressings, search for other solutions possessing some of its qualities and adapted for these uses must be made.

### SUMMARY

The composition and properties of a new antiseptic solution that is neither toxic, irritant nor allergenic are described. A comparison between it, tincture of iodine and five commercial antiseptic solutions by the agar-cup plate method, with the use of twelve commonly occurring micro-organisms, demonstrates its bactericidal efficacy. Its chemical, physical and bactericidal properties seem to commend its use in mixed infections of the skin and mucous membranes.

Although the perfect antiseptic for topical application in mixed wound infections has not yet been discovered, carbamide peroxide in glycerol or similar solutions appears to approach this goal.

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## PAPILLOMA OF THE GALL BLADDER\*

DAVID MILLER M D †

NEW YORK CITY

**I**N THE general problem of biliary disease, the relatively infrequent occurrence or recognition of papilloma of the gall bladder is of interest. This report was prompted by the recent finding of 3 cases within the last few months. In each case the preoperative diagnosis was correctly made by the roentgenologist.

Estimations of the frequency of occurrence of papillomas vary, depending on the criteria for histologic diagnosis of these tumors. Kerr and Lendrum,<sup>1</sup> whose criteria were most exacting, had accepted only 7 cases up to 1936. To these was added a case reported by Brown and Cappell<sup>2</sup> and accepted by the previous authors. On the other hand, in the American literature, Irwin and MacCarty<sup>3</sup> found 85 cases of papilloma of the gall bladder in 2168 cases of gall-bladder disease, and C. H. Mayo<sup>4</sup> found 107 cases in 2538. Kirklin<sup>5</sup> reported an incidence of 8.5 per cent of gall bladders containing one or more papillomas in 1700 patients undergoing cholecystectomy at the Mayo Clinic during a period of about six years. Recently, Greenwald<sup>6</sup> reported a series of cases similar to those discussed below.

Although polypoid lesions of the colon and the urinary bladder have a significant association with carcinoma of these organs, this does not appear to be important in the present connection. Phillips<sup>7</sup> in his series of 500 cases found 1 case in which carcinoma occurred in a papillomatous gall bladder. Kerr and Lendrum<sup>1</sup> reported 3 cases of carcinoma in patients who had gall bladders containing papillomas. I am not aware of any other similar cases.

In the following cases, the abdomen was surgically explored and the gall bladder was removed because of the presenting symptoms, rather than because of the possibility of cancer. The latter can never be ruled out, however, without histologic examination. It is not unreasonable to expect that in rare cases an early carcinoma near the fundus of the gall bladder will be found in cases in which the preoperative diagnosis is papilloma.

## CASE REPORTS

**CASE 1.** A. K. W. (DH-40999), a 36-year-old, married woman was admitted on July 27, 1944, complaining of attacks of nonradiating pain in the right upper quadrant of the abdomen of 3 years' duration. The attacks occurred at 2-month intervals and followed the ingestion of fatty or fried foods. There had been no fever, chills or jaundice. Twelve years previously, the patient had a cesarean section. She had had no other operations and no significant illnesses.

Physical examination was essentially noncontributory. Roentgen-ray examination by Dr. Alice Ettinger at the Pratt Diagnostic Hospital, Boston, revealed papillomas of the gall bladder.

\*From the Surgical Service of Dr. Ralph Colp, Mount Sinai Hospital.  
†Adjunct surgeon, Beckman Hospital, member of staff, out-patient department, surgical clinic, Mount Sinai Hospital.

The patient was operated on by Dr. Ralph Colp. Exploration of the abdomen revealed a gall bladder of normal size with a slightly thickened wall. Cholecystectomy and appendectomy were performed.

Gross examination of the mucosal surface of the gall bladder showed four papillomas, each 0.5 cm. long, attached by thin pedicles. They were the same color as the rest of the mucosa and somewhat translucent. Microscopic examination of these tumors showed tufts of thin stroma lined with columnar cells (Fig. 1), some of the tufts were stuffed with large clear lipid-

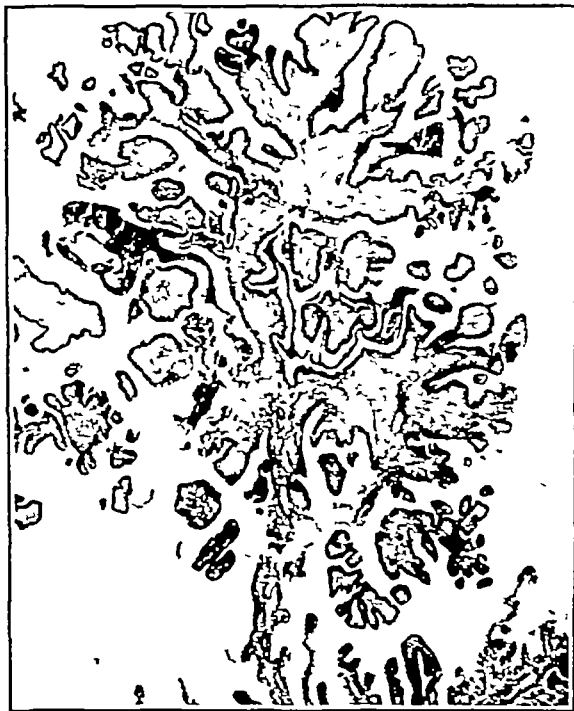


FIGURE 1 Case 1

*A low-power photomicrograph showing the papilloma attached by a thin pedicle to the mucous membrane of the gall bladder.*

bearing cells. The surface epithelium of the gall bladder mucosa was otherwise normal. The wall of the organ showed an increase in fibrous tissue and round cells. The appendix was normal on gross and microscopic examination.

The patient was relieved of her symptoms and made an uneventful recovery.

**CASE 2.** D. B. (DH-42485), a 46-year-old, married man, was admitted in November, 1944, complaining of attacks of pain in the right upper quadrant of the abdomen, radiating to the right shoulder and scapular region, of several months' duration. For an indefinite period of time he had had postprandial distress and flatulence. On rare occasions he had had some nausea and vomiting. He had never had fever or jaundice with attacks of pain. The past history revealed nothing of importance except hay fever.

Physical examination was essentially normal except for slight tenderness in the right upper quadrant. Roentgenograms of the gall bladder were interpreted by Dr. Arthur Bendick as showing papillomas.

Exploratory laparotomy was performed by Dr Ralph Colp on November 9. The gall bladder was distended with dark-green bile and contained several stones. When it was removed and opened, it was seen to contain two papillomas 1 cm in length. Microscopically, these consisted of piled-up villi with a thin fibrous core lined with columnar epithelium (Fig. 2). The wall of the gall bladder and the mucous mem-



FIGURE 2 Case 2

*A low-power photomicrograph showing the papilloma, which has complex processes*

brane were otherwise normal. The common duct was not dilated and contained no palpable stones. There were no other abnormalities.

The patient recovered from the operation uneventfully and has been well to the present.

**CASE 3** J. M. (MSH-431865), a 35-year-old man, who was admitted in March, 1945, had had vague episodes of dyspepsia over a period of 8 months. These were unrelated to the ingestion of any particular foods. Three weeks before admission he had an attack of epigastric pain, which was relieved by the repeated belching of gas. Similar attacks ensued at irregular intervals. Six hours before admission, non-radiating epigastric pain and distress began and persisted. There was no vomiting.

On physical examination there was moderate tenderness in the right upper quadrant of the abdomen. The patient was afebrile. No mass was palpable. The white-cell count was 16,000, with 90 per cent neutrophils.

The patient was given intravenous glucose and saline solution, and the symptoms subsided within a few hours. Subsequent roentgen-ray examination of the gall bladder showed two radiotranslucent areas, which did not shift in position as the patient was moved (Fig. 3). Dr Marcy Sussman's diagnosis was papilloma of the gall bladder.

The patient was operated by Dr Ralph Colp on March 20, 1945. The gall bladder was thin-walled. The stomach was normal. The gall bladder was removed and opened, and two papillomas of split-pea size were seen on the mucous membrane, to which they were attached by thin pedicles. There was an elevated area of mucous membrane 0.5 cm in diameter above the surface of the mucosa. There were also present two bright-orange excrescences 1 to 2 mm in diameter. There were no stones.

The patient has remained well since operation.

## DISCUSSION

The etiology of these tumors is a matter of speculation. Infection may play a significant part. Of the 500 cases reported by Phillips,<sup>8</sup> 255 (51 per cent) occurred in association with chronic catarrhal cholecystitis. In contrast to carcinoma of the gall bladder, the presence of stones in papilloma of the gall bladder seems to have no etiologic significance. Stones were present in 26.8 per cent of Phillips's series. Carcinomas of the gall bladder are associated with stones in 65 per cent to 90 per cent in various series. Polypoid excrescences occur in the so-called "strawberry" gall bladder. These contain deposits of cholesterol, discernible to the naked eye as yellow masses. Such masses may form the nuclei for stones.

Phillips<sup>8</sup> states that infection and metabolic disturbances, often working together, may play a role in the etiology of these tumors. The nature of the metabolic disturbance is not clear. In a number of cases described by him, papillomas were present in a strawberry gall bladder.

The papillomas appear as projections from the mucous membrane of the gall bladder. Their composition is that of the mucous membrane. The pedicles may be so thin that the new growth is easily brushed off or so broad that the mass is firmly attached. These projections may appear in any portion of the organ, but they occur oftenest at its neck or midportion. Microscopically the growths consist of branching complex processes of thin stroma lined with columnar cells.

In the large series of reported cases, the majority of cases usually occur after the third decade of life. The ages in the present cases were thirty-five, thirty-six and forty-six years, respectively.

The symptoms that bring the patient under observation are similar to those of chronic cholecystitis. Intolerance to fatty or fried foods, dyspepsia, flatulence and attacks of pain in the epigastrium and right upper quadrant of the abdomen occur. Fever, chills and jaundice are not usually noted. The patient comes to operation at any time from months to years after the onset of symptoms. It is not clear why these papillomas, often unassociated with stones or infection, produce symptoms. One is forced to indict a vague metabolic disturbance as a causative agent. Relief of the symptoms is obtained by cholecystectomy.

The preoperative diagnosis can be readily made with a high degree of assurance by roentgen-ray examination. In a series of 15 cases of papilloma, Kirklin<sup>6</sup> was able to diagnose 14 preoperatively. He states that the best time for examination is the twentieth hour after the ingestion of dye. Stones usually change their position with succeeding examinations, are often bunched together and are most frequently found at the fundus. Most papillomas are discrete, do not change position and are

rarely found at the fundus. Adenomas are usually larger than papillomas, measuring 2 cm or more in diameter, as against 0.5 cm to 1.0 cm, and are frequently present at the fundus. Sarcomas are exceedingly rare, only 13 cases having been recorded in the literature.

Since the majority of carcinomas arise near the neck of the gall bladder, the organ is obstructed and damaged and cannot be accurately visualized.

When the papillomas give rise to symptoms, the treatment is surgical. Cholecystectomy should be performed, since it gives relief. Unless jaundice has been noted preoperatively or operation reveals a dilated common duct with an intrinsic palpable mass or many small stones, the common duct need not be opened. Colp<sup>11</sup> pointed out in a recent paper that between 30 and 40 per cent of cholecystectomized patients have attacks of pain similar to those

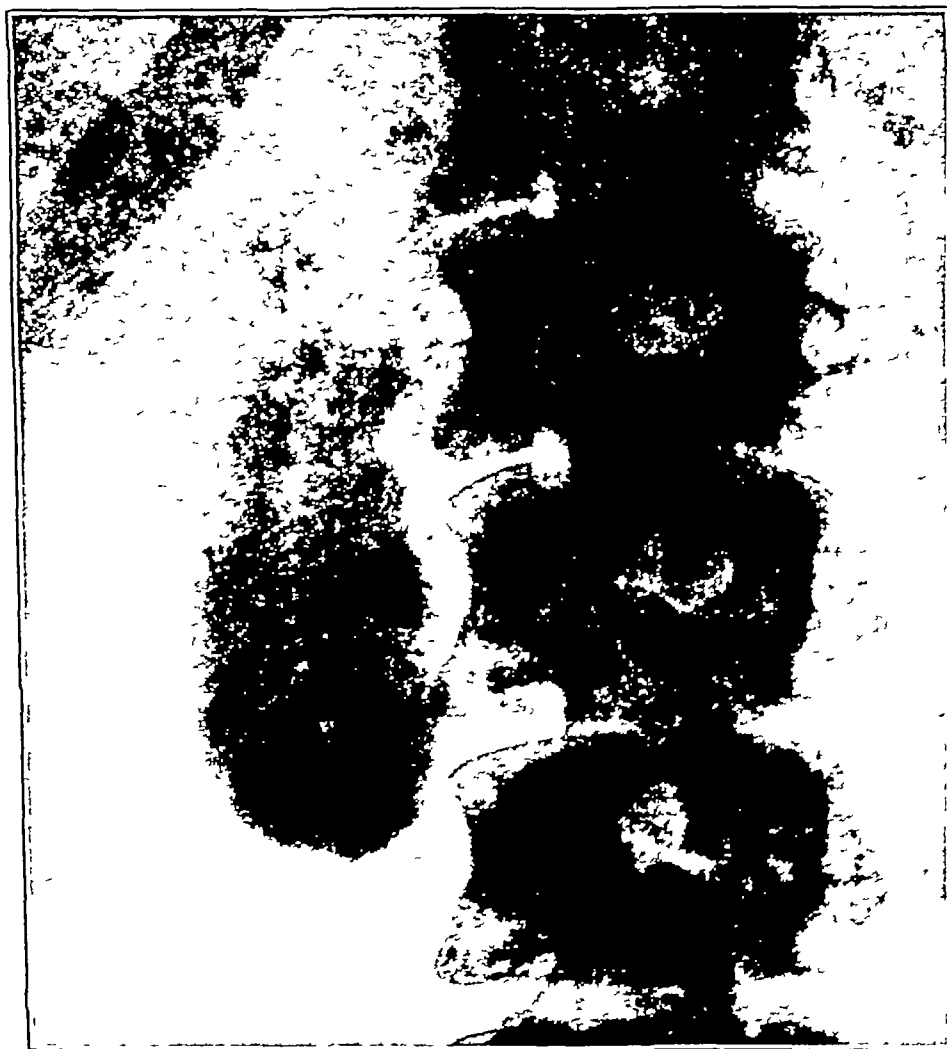


FIGURE 3 Case 3  
Gallbladder at twenty-one hours filled with dye and showing two faint translucent areas

Sosman,<sup>9</sup> in his recent excellent paper on the radiologic aspects of gall-bladder disease, stated that he had never made a diagnosis of carcinoma of the gall bladder by cholecystography. Furthermore, Sussman<sup>10</sup> does not recall having made such a diagnosis. For details of the technic of cholecystography, the papers by Sosman<sup>9</sup> and Kirklin<sup>5</sup> should be consulted.

that preceded operation. These attacks usually occur within two years of the operation and may be temporary. In cases in which stones had been present, this postcholecystectomy syndrome was encountered less frequently.

#### CONCLUSIONS

<sup>1</sup> Papillomas of the gall bladder are rarely associated with carcinoma.

Exploratory laparotomy was performed by Dr. Ralph Colp on November 9. The gall bladder was distended with dark-green bile and contained several stones. When it was removed and opened, it was seen to contain two papillomas 1 cm in length. Microscopically, these consisted of piled-up villi with a thin fibrous core lined with columnar epithelium (Fig. 2). The wall of the gall bladder and the mucous mem-



FIGURE 2 Case 2

*A low-power photomicrograph showing the papilloma, which has complex processes*

brane were otherwise normal. The common duct was not dilated and contained no palpable stones. There were no other abnormalities.

The patient recovered from the operation uneventfully and has been well to the present.

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lowing discharge, or are followed in their homes by visits at intervals of a week to a few times a year. Lichtenstein describes his method of treatment as follows

Fresh cases receive from the outset "free diet" [By this Lichtenstein means a diet completely corresponding with that of healthy children] The diabetic children are allowed at first to take the ordinary hospital fare and eat their fill. In their homes they are then allowed to share the diet of their brothers and sisters and playmates and to satisfy their individual taste within the same limits as for healthy children. Even sugar and sweets in reasonable amounts are permissible. At the hospital the amounts of food which the children spontaneously consume are weighed and measured. In their homes no weighing or measuring of the food is required. The only restriction made is to avoid overindulgence, a rule that should apply in equal degree to all children, thus also to healthy ones.

The children receive the amount of insulin required to produce a good general condition, a feeling of well-being, a satisfactory increase in weight, a moderate amount of urine and complete freedom from acids in the urine. On the other hand, I attach less importance to a moderate rise in blood sugar and to a moderate or small excretion of sugar, in itself. Indeed, I prefer some excretion of sugar to complete freedom from sugar in the urine, as one then runs a smaller risk of hypoglycemia and ketosis, the two dangers that in the first place menace the diabetic child.

The transition between dietetic treatment and "free diet" could always be made without difficulty. Thus children who had previously received a diet of less than 100 gm of carbohydrate per day, during the first few days of the "free diet" consumed 250 to 300 gm of carbohydrate per day. After a few days, however, they spontaneously adjusted themselves to a more moderate consumption of carbohydrates, which, however, was always considerably higher than the amount previously permitted. As a rule it was about 150 to 250 gm per day, corresponding to 6 or 7 gm per kilogram of body weight.

These children spontaneously consume as a rule 2 or 3 gm of protein and 2.5 to 3.5 gm of fat per kilogram per day. The supply of calories was as a rule spontaneously maintained at 80 to 100 for children under five, at 60 to 80 at the age of five to ten years and at 40 to 60 at the age of ten to fifteen years, all per kilogram of body weight.

The general condition of the patients is recorded throughout as extremely satisfactory, with no increased hunger, thirst or polyuria. They are said to have had a feeling of well-being and joy of life, in contrast to the regime that marked them out from healthy children. Growth in height and weight, with a few isolated exceptions, were well within the normal limits for healthy children in Sweden. No difficulties were encountered during puberty. As regards the carbohydrate metabolism, the presence of sugar in the urine up to some tens of grams of sugar for twenty-four hours was not considered a cause for concern provided that the patients felt well, and showed no increase in hunger or thirst, polyuria or itch. As a rule, the degree of glycosuria was less than 10 per cent of the carbohydrate intake. As a result of these measures, severe attacks of hypoglycemia were, in fact, extremely rare.

The blood-sugar fasting values in most well controlled cases ranged between 100 and 200 mg per 100 cc.

Lichtenstein believes that the patients reacted better to infections than they did on the previously restricted diets. There was only 1 death from military tuberculosis, and of 41 patients who sooner or later

showed a positive tuberculin reaction, only 1 developed a lung focus, and this healed. Neither increase in blood pressure nor demonstrable calcification of the blood vessels was observed. The cholesterol, as a rule, was below 230 mg per 100 cc. In 1 case there was a slight unilateral cataract, and in a number of cases there was a slight transient enlargement of the liver.

Lichtenstein's mortality was low. Of the 169 patients, only 8 died. One was murdered, 1 succumbed to military tuberculosis with meningitis a few months after the onset of diabetes, 1 died of pleural empyema with peritonitis and one of scarlet fever, 1 died of oral infection, and 3 died of coma. The mortality rate for the ten-year period was 4.7 per cent. Lichtenstein compares this rate with that of my cases, as reported by White,<sup>50</sup> which was 8 per cent for 150 cases of fifteen years' duration. A comparison to be valuable should be made between children with similar durations of diabetes. It should be added that the mortality of this clinic will be still higher in the 249 cases that are of twenty years' duration and are soon to be reported.

Hagedorn's protamine insulin was used in Lichtenstein's cases instead of protamine zinc insulin. The dosage varied between 10 and 120 units a day, the average being about 40 units. The maximum dose of regular insulin averaged about 60 units. Lichtenstein also frankly points out

To obtain good results, one must exercise a careful, continuous control, with at first frequent and gradually more occasional examinations. In the case of children, the control involves good co-operation with the homes, especially with the mothers. It is therefore necessary to give instructions to the mothers. They must learn the principal features in the clinical treatment of the disease, they must learn to recognize, in particular, such changes in the child's condition as require a modification of the insulin dosage, and they must learn to use the insulin syringe correctly. Many mothers in our Swedish clientele can be taught to make qualitative and sometimes also quantitative sugar tests and even to perform Gerhard's and Legal's tests for ketone bodies in the urine. A more important matter, however, is to draw their attention to the significance of *greater thirst* and *large amounts of urine* as indications of unsatisfactory adjustment, and to the importance of immediately getting in touch in such cases with the doctor treating the case. Another important matter is to get the mothers to understand the *signs of hypoglycemia* and how it is counteracted. The importance of a *regular conduct of life* with regular meals should also be strongly emphasized.

My own aversion to the treatment advocated by Lichtenstein arises not so much from the actual diets that he employs — which, as a matter of fact, differ little from the average diet now generally given to diabetic children — as from the psychologic effect on the children and the parents of growing up with the belief that their diabetes can be controlled by insulin and not by diet, insulin and exercise. It is the old, old story — a compromise with evil that a possible good may come. Seneca wrote, "We may lay it down as an invariable axiom in all high education that it is never sensible to permit what is bad for the supposed sake of preventing what is worse." In the education of his pupil Nero,

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so good a man as Seneca adopted this course but the world knows with what disastrous results. There is unanimous belief among my group that the children who have been treated with great care on a diet including 150 to 200 gm of carbohydrate and who have endeavored to control their diabetes are the ones who have done the best and have avoided the most complications. I know—and my colleagues agree with me—that the patients who have lived on free diets but have admittedly tried less earnestly to control themselves with insulin have been the ones most frequently admitted to the hospital for coma and hypoglycemia. The extremes of such cases will not be included in our twenty-year group, soon to be reported, because these patients are already dead—they did not live even for twenty years.

Long ago I found on visits to noted diabetic clinics in this and other countries that the physicians in charge were skilled clinicians and treated their patients individually and with good results. These clinicians might advocate particular methods of treatment, but in their own clinics they were alive to the individualization of the patient and adjusted the diet and the giving of insulin accordingly. I suspect that this is the case with Lichtenstein, but I also believe that, if he should visit our diabetic camp for girls, he would be impressed with the joyous natures of the campers and would find that they were being given prescribed diets not so very different from those served in their homes by the mothers of his own children, for his intelligent Swedish mothers undoubtedly found that restricted diets worked the best.

#### STATISTICS ON DIABETES IN FINLAND

The Vartiainens<sup>51</sup> estimated the number of diabetic patients in Finland and at the same time noted the variations in distribution according to age, sex and place of residence—urban or rural. They reached the conclusion that in 1942 the number of such patients was 5800, or 1.6 per 1000 of the total population, which is reported as 3,637,354. If this estimate were applied to the United States, it would mean less than 250,000 such patients. The Vartiainens' estimate is actually based largely on the number of persons receiving aid on account of diabetes, but it is rendered incomplete by the fact that a certain percentage of the inquiries remained unanswered, and by the fact that a large percentage of persons living in the country districts do not require aid of this sort. Without allowing for incomplete replies, chiefly in the urban districts, the Vartiainens reached an estimate of 2703 diabetic patients, but decided that a more nearly correct figure would be 2834. Adding to this number those whose occupations were on farms and in fisheries, they increased their estimate to the final one of 5800.

At the First University Medical Clinic in Helsinki the yearly number of cases treated varied widely,

reaching a peak in the five-year period 1930-1935 and suffering a marked drop in the ensuing five years. They evaluated this variation as partly indicative of the interest of physicians or the preferential admission of patients to the hospital, because in the Second University Medical Clinic the figures were dissimilar.

Comparison of the diabetic mortality computed by insurance companies in Finland with the total mortality of the country gave the surprising result that the percentage of diabetic deaths remained practically constant at 1 per cent from 1890 to 1940, showing only an insignificant drop in the last five years of this period. Information from this source should probably be disregarded, since even in our country it is apparently not considered of great value.

The total diabetic mortality in Finland from 1927 to 1941 showed a steady increase. The number of deaths among males remained nearly stationary, but that among females nearly doubled, the deaths being confined chiefly to patients fifty years of age or above.

The estimated figure of 5800 diabetic patients in Finland, or 1.6 per 1000 population (1 patient among 667 persons), is far lower than the generally accepted incidence in the United States, which is at least 1 patient among 150 inhabitants. Perhaps the methods of computing mortality statistics in the two countries are different. It is said that in 1936 nearly 12 per cent of all deaths in Finland were ascribed to senility and an additional 2 per cent to unknown causes. Moreover, the mortality from tuberculosis was twenty-five times as high as that from diabetes. Some diabetic patients may have been in such groups and thus not included in the estimate.

#### DIABETIC ASSOCIATIONS, SOCIETIES, FOUNDATIONS AND TRUSTS

Compared with tuberculosis and cancer, diabetes is far behind in the support that it receives from associations, societies, foundations and trusts, yet the need for such support is manifest. There are certainly close to 1,000,000 living diabetic patients in the United States today. Diabetes ranks eighth in the causes of death, and in 1940 it was responsible for 1 death in every 40. Tuberculosis is decreasing, but diabetes is increasing, owing to the prolongation of life in the general population to the age at which the onset of diabetes is most frequent, and owing to the longer duration of life of such patients. One often speaks of childhood diabetes, forgetting that four or more times the life of the diabetic patient with onset in childhood will be lived as an adult.

Centers are needed for experimental investigation, the conducting of statistical studies and the stimulation of physicians in the surrounding communities. Emergency diabetic stations are needed in all large hospitals, hospitals must be properly equipped, and communities must be protected by an



extension of education in the treatment of the disease through hospital classes and outpatient departments. Above all, laboratory facilities must be extended to the practicing physician, because it is he who sees and treats most of the diabetic patients.

The Diabetic Association was inaugurated in London in 1934. The number of members has steadily grown to a total of 8400. Under the auspices of the association *The Diabetic Journal*, now in its fourth year, is issued every three months at the price of 1 shilling an issue. The Diabetic Association thus far is particularly a lay organization, conducted for the benefit of diabetic patients. During the war period it exerted much influence and was of great value to the country in bringing about the system of identification cards for diabetic patients, securing proper rations, making provision for such patients who were rendered homeless and helping to provide a home for diabetic children. It has issued a diabetic cookbook, presents occasional broadcasts on the radio, and is now interested in establishing a Banting Memorial Home. The honorary president is the noted author, H. G. Wells. The driving force among the medical profession has been Dr. R. D. Lawrence.

One of the earliest foundations for diabetes in the United States was the George S. Cox Medical Research Institute, established in 1931 at the University of Pennsylvania in Philadelphia. It is in the Hospital of the University of Pennsylvania, within the Department of Medicine. Dr. C. N. H. Long became the first director in 1932 and served until 1936. He was succeeded by Dr. F. D. W. Lukens, who has served from 1936 to the present time. The staff, in addition to its research work, conducts the outpatient section for diabetes of the Medical Clinic. The laboratory has contributed studies on the physiology and pathogenesis of diabetes. In the clinic, studies on immunity and of the value of exercise and other clinical observations have been made.

For eight years, — from 1934 through 1942, the children of the clinic were sent to the University Camps at Green Lane, where they were supervised by the staff with the assistance of specially trained medical students. This valuable activity was interrupted by the war but will be resumed as soon as possible.

The Renziehausen Foundation was opened on January 1, 1938, in the Children's Hospital of Pittsburgh. It was established through a gift from Miss Emily Renziehausen, of Pittsburgh, for the purpose of taking care of diabetic children. These patients are admitted without charge and are kept under continuous medical and educational supervision up to the age of sixteen. Connected with this foundation is a convalescent home at Large, Pennsylvania, to which children can be sent during the warmer months of the year. The staff of the foundation is made up of members of the faculty

of the Medical School of the University of Pittsburgh and of nurses who are specially trained in pediatrics and diabetic work. Also, the Renziehausen Ward is used for the teaching of medical students and social-service workers. Both the children and parents are taught to know as much about diabetes as possible, and home conditions requiring improvement are usually corrected. Patients are accepted regardless of race, color, creed or financial status, up to the capacity of the foundation to give them proper care.

The New York Diabetes Association was established in New York City in 1934 through the efforts of Drs. Charles Bolduan and Herman O. Mosenthal, with the financial aid and the endorsement of Lucius Littauer. It was affiliated with the New York Tuberculosis and Health Association for three years, and then became independent, with offices at the New York Academy of Medicine. Drs. Herman O. Mosenthal, James Ralph Scott, Charles F. Bolduan, George E. Anderson and Frederick W. Williams have successively been presidents of the association.

The activities of the association have included the publication of *Fundamental Concepts*, which are pamphlets on various phases of diabetes. These have been widely distributed to the profession and to medical schools. A children's camp has been conducted since 1936. At first, the camp accommodated 30 children for a two-week period each. In the summer of 1945, 100 children were taken for a period of four weeks, each, and for 1946 a permanent site, with buildings accommodating approximately 250 children during the summer, has been acquired.

Research projects have been established during the last eight years, and numerous publications have resulted from them. Scientific meetings for physicians and lectures for the laity have been successfully carried out. The latest project of the New York Diabetes Association has been to found the Clinical Society of the New York Diabetes Association. This has secured a large membership among the physicians of Greater New York. This society holds meetings for physicians, is certifying specialists in diabetes in its area, and is taking steps for the standardization of diabetic clinics.

In Cincinnati in 1935, an organization for diabetes was begun. It was established under the name of the Council on Diabetes of the Public Health Foundation. It has led an active existence. Statistical studies have been made, public meetings have been held from time to time, and special posters and exhibits have been prepared and distributed. In 1939, a diabetes instruction service was inaugurated for the benefit of physicians who had the care of diabetic patients in the low income group. Refresher courses for nurses and physicians were established, and a radio program on diabetes was presented in a Sunday evening series. Letters sug-

gesting the possibility of employment of controlled diabetic patients were sent to the directors of industries. Diabetic identification cards were distributed, and a camp was operated for children. At one time an inventory of diabetes in the local schools was made, with the result that a sample survey of 5800 children disclosed only 3 diabetic children, thus indicating a number too small to warrant such an extension of the project to the entire school system.

The American Diabetes Association may be said to have been an outgrowth of the Cincinnati society. Dr. Cecil Striker, of Cincinnati, served as its first president and continues to be its efficient activating force. The first annual meeting was held in June, 1941, but the constitution of the association was adopted on June 12, 1940. Yearly meetings have been held, and the reports of the association's activities and papers read have been published. A notable contribution to the control of diabetes throughout the world has been the issuance of *Diabetes Abstracts*. This quarterly is published by the association and is financed with the help of the Eli Lilly Company. It contains abstracts of all articles on diabetes appearing in medical journals throughout the world. The membership of the association now exceeds 750.

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sponded generously to solicitation, and at the present moment \$243,000 has been received from 3112 persons for extension of the facilities of the hospital along diabetic lines. It seems particularly desirable that this plan of securing gifts from the many and not from the few should be cultivated, and it is the hope of those inaugurating the diabetic funds at the Boston Safe Deposit and Trust Company and the diabetic projects at the New England Deaconess Hospital that the example set will be followed in other localities.

It is a sign of the increasing interest in and importance of diabetes that in the plans for the addition to the Rhode Island Hospital in Providence \$54,000 has been set aside for the Diabetes Clinic.

Active work in diabetes is in progress in a multitude of hospitals and laboratories. I hesitate to publish the above list of societies, but do so partly with the idea that this will lead to corrections and

amplifications, which I shall receive with gratitude. At the Mayo Clinic, in St. Louis, in Omaha, Nebraska, at the University of California and in various hospitals in Chicago extremely active diabetic investigation is going on. Diabetic camps have been conducted at various times in connection with work in the above localities, and continuously at the University of California since 1938. I understand that a diabetic trust fund is in process of creation in Portland, Oregon, and that an organization of somewhat wider scope is being formed in Omaha.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

#### CASE 32141

##### PRESENTATION OF CASE

A sixty-year-old housewife was admitted to the hospital because of jaundice.

A year and a half before admission the patient became weak and lethargic and had mild anorexia. She remained in bed for several weeks and slowly regained strength until four months before admission, when she became insidiously tired and was noted to have jaundice. Her skin itched slightly, and her urine became dark. Her appetite disappeared. At the height of the jaundice a Graham-Cole test was unsuccessfully attempted by her physician. On a low-fat, low-calorie diet the jaundice slowly disappeared, but it recurred one month before admission. At that time she had two episodes a week apart of sudden acute colicky pain in the right upper quadrant. Each attack lasted half an hour and was not associated with nausea or vomiting. She had had no chills or fever at any time. During that month she was given iron and liver for anemia. The iron was stopped four days prior to

admission, and after that her stools were clay colored. The color of the stools had not been observed previously. There had been a 25-pound weight loss in the four months prior to admission. There had been no swelling of the abdomen or ankles at any time.

The patient had been jaundiced as a child. Seven years before admission an appendectomy had been performed. Prior to the onset of jaundice it was routine for the patient to have one or two cocktails before lunch and dinner and a highball at bedtime. Thereafter her appetite for alcohol decreased proportionately with her desire for food so that she had only an occasional cocktail at noon.

On physical examination the patient was thin and sallow, with a yellowish-brown skin and yellow scleras. There were Grade I apical and aortic systolic murmurs. The liver was palpable in the right hypochondrium and in the epigastrium, the edge was tender and round and the surface was questionably nodular. The tip of the spleen was palpable. There was a firm round mass in the right upper quadrant, immediately beneath the liver edge.

The temperature was 98.6°F, the pulse 75, and the respirations 20. The blood pressure was 132 systolic, 76 diastolic.

The hemoglobin was 12.8 gm. The white-cell count was 8800, with 59 per cent neutrophils, 28 per cent lymphocytes, 7 per cent monocytes and 6 per cent eosinophils. The urine had a specific gravity of 1.028 and gave a ++ test for albumin and a +++ test for bile. The sediment contained 25 white cells and 10 epithelial cells per high-power field. The test for urobilinogen was positive in a dilution of 1:100. The prothrombin time was 30 seconds (normal, 18 seconds), and the serum protein 6.7 gm, with an albumin globulin ratio of 2:1.

The nonprotein nitrogen was 29 mg per 100 cc, and the alkaline phosphatase 26.7 Bodansky units. The stools varied from brown to clay colored and from strongly to slightly positive for bile, they were guaiac negative. During the Graham test the gall bladder contained poorly concentrated dye and was not well visualized, it appeared to contract after a fat-containing meal. No stones were seen. Fluoroscopically the stomach contained a questionable filling defect close to the cardia in the lesser curvature. The stomach was long and low in position. The second portion of the duodenum lay considerably more to the right than usual, and there was a suggestion of a filling defect at the junction of the second and third portions. So far as could be demonstrated the duodenal loop and head of the pancreas were readily movable. At the end of six hours the barium was scattered through the terminal ileum and colon.

On the sixth hospital day the patient had an attack of biliary colic and the jaundice increased.

An operation was performed on the eighth hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR WYMAN RICHARDSON: This is a case of jaundice, and it presents the same old problem of deciding whether it was intrahepatic or obstructive, or both. Let us briefly review the clinical history for a moment. I have no answer for the lethargy and weakness, which were present one and a half years before entry, as part of the present illness. It makes some difference regarding the ultimate diagnosis. The skin itched slightly at the time of admission, and the urine became dark. Although it says "slightly," that may be of some importance, and as you know it suggests biliary obstruction rather than intrahepatic jaundice. At the height of the jaundice the Graham-Cole test was unsatisfactory. I believe that it is usually considered rather pointless to try to visualize the gall bladder by x-ray in the presence of deep jaundice. Is that so, Dr Lingley?

DR JAMES R LINGLEY: Yes.

DR RICHARDSON: The low-fat diet was all right in the presence of jaundice, but I should say that a high-protein, high-carbohydrate, high-calorie diet containing numerous supplementary vitamins was indicated rather than a low-calorie diet. The pain is described as colicky, but it appeared to be of brief duration.

I "saw red" when I read that both iron and liver were given for anemia. This is done frequently, but if the anemia improves, one does not know whether the improvement was due to the giving of liver or to the giving of iron. It is rare that both iron and liver need to be given to the same patient.

"The patient had been jaundiced as a child." I take it that that means an episode of jaundice and not prolonged jaundice throughout childhood. It

could be interpreted as infectious hepatitis, and one may consider that a previous attack of infectious hepatitis may predispose the liver to damage later on. There is some evidence of this fact in a paper published by Dr Altschule and Dr Gilligan.\* To me the evidence is not entirely convincing, since it is based on certain tests some of which, it seems to me, are not entirely specific for liver failure.

There is a slight alcoholic aroma to the history. That may be put in to make it difficult to decide about the question of the cause of this jaundice.

The patient had a yellow-brown skin. I do not know the nationality.

DR TRACY B MALLORY: She was Irish.

DR RICHARDSON: The yellow-brown skin is suggestive of biliary obstruction rather than intrahepatic jaundice.

The "questionably nodular" liver leaves me cold. I think that it is extremely difficult to feel a nodular liver through an abdominal wall. One may feel a grossly nodular liver, such as occurs in the hepatic lobatum of syphilis, and with especially big tumor nodules one may get the impression that the liver is irregular, but, as I have said, a questionably nodular liver means nothing to me.

The fact that the tip of the spleen was palpable is of great importance, and if that notation appears on the record one can usually accept it. In other words a positive finding seems to me more important than a negative finding, especially regarding the spleen.

The firm round mass in the upper quadrant could well have been a dilated gall bladder, although it is frequently difficult to feel a gall bladder and sometimes it does not give the impression of being firm.

The 12.8 gm of hemoglobin indicates a slight anemia. It is perhaps a definite one, even though this patient was a woman. The blood differential was normal. I shall assume that the 6 per cent eosinophils was within the normal limits. The urine was essentially normal, except for the fact that bilirubin was being passed through the kidney. There were a few white cells, but I do not believe that they were significant.

Urobilinogen was present in the urine in a dilution of 1:100. That is definitely increased and means, according to my own definition, that bilirubin was excreted into the gut, because as I understand it, urobilinogen is formed from bilirubin only in the gut, it is reabsorbed and excreted normally through the kidney to some degree, but it may be excreted in increased amounts when there is an increased load of bilirubin going through the biliary system. It may also be increased in some cases when there is inability on the part of the liver to excrete urobilinogen, whereas at the same time the liver can excrete bilirubin. That is confusing. The point is that the presence of increased uro-

\* Altschule, M. D. and Gilligan, D. R. Chronic latent hepatitis following catarrhal jaundice. *New Eng J Med* 231:315-317, 1944.

bilinogen in the urine should be a great help, but it frequently is not. In this case it is corroborative evidence that bilirubin was being excreted through the biliary tract into the gut.

The prothrombin time was slightly elevated, and the serum protein was normal. The normal albumin-globulin ratio suggests that there was no considerable degree of intrahepatic disease. The alkaline phosphatase was distinctly elevated, which is in favor of biliary obstruction and somewhat in favor of neoplastic disease.

I want to ask Dr. Lingley whether the head of the pancreas ever is movable. I had not supposed that it was.

DR. LINGLEY: I should not expect it to be.

DR. RICHARDSON: I wonder why it said "readily movable."

DR. LINGLEY: I believe that it is a mistake that the examiner meant the duodenum, rather than the pancreas.

DR. RICHARDSON: Is there or is there not a peptic ulcer in the midportion of the duodenum? The report is mildly suggestive. Would you interpret that as being questionable?

DR. LINGLEY: Yes. The second portion of the duodenum is sometimes difficult to examine because you cannot fill it completely. Small lesions may be hard to demonstrate and in this case I judge that there was some question about it in the examiner's mind.

DR. RICHARDSON: Is there any other comment that you would like to make?

DR. LINGLEY: In regard to the gastric filling defect, the left lobe of the liver can push over against the stomach immediately beneath the cardia and produce a pressure defect where this one is described.

DR. RICHARDSON: I think that the evidence is strong that this patient had a biliary obstructive lesion. The question is, Was it a ball-valve effect or was there a partial obstruction that allowed a certain amount of bile to get through but not the normal amount? Can we rule out intrahepatic disease? I do not believe that one can completely rule it out, but it seems to me that the clinical history is opposed to it, except for the use of alcohol. There was no edema, ascites or varices, and the serum protein was normal. The prothrombin time can be elevated in either condition. There is no note whether the prothrombin time returned to normal after the administration of vitamin K<sub>1</sub>. If it did, it might be of some value in indicating that this was an obstructive lesion.

What type of lesion was it? I think that in the wards we frequently have a grand guessing match and end up by operating on the patient to find out. I sincerely believe that any patient with biliary obstruction should be operated on, even though the probability of a malignant tumor may be strong. I remember one patient who was not operated on and whom Dr. Mallory finally examined, only to

find a miserable little stone in the mouth of the common bile duct. As between obstruction, tumor and stone, in favor of tumor are the enlarged gall bladder, the considerable increase in the alkaline phosphatase and the appreciable weight loss. In favor of stone is the history of colicky pain, which I think may occur with either condition but is nevertheless suggestive of stone. We are told that in the presence of stone the gall bladder is usually small and not large. The palpable spleen is not much more in favor of stone than it is of malignancy, but it is suggestive of intrahepatic disease.

Finally, should one consider the possibility of a peptic ulcer in the region of the ampulla, which had caused constriction and resulted in an obstructive lesion? That does occur rarely, but I should expect it to occur in a chronic, long-standing ulcer, of which there is a little evidence in this patient.

I cannot think of any other way to narrow this down. I think that this patient had a malignant tumor, probably arising in the pancreas. It is possible that she had both some type of obstructive lesion and intrahepatic disease, but I am not going to complicate matters by saying that. I will say that there was no intrahepatic disease other than that associated with biliary obstruction, a beginning biliary cirrhosis, if you will. I believe that it is more usual to have intermittent jaundice with stone than with tumor, although I think that it does occur with the latter. My final diagnosis is, as I have said, malignant tumor, probably carcinoma of the head of the pancreas.

#### CLINICAL DIAGNOSIS

Carcinoma of head of pancreas

#### DR. RICHARDSON'S DIAGNOSIS

Malignant tumor, probably carcinoma, of head of pancreas

#### ANATOMICAL DIAGNOSIS

Carcinoma of ampulla of Vater

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: I am sorry that Dr. Chester M. Jones was called away. I had hoped that he would discuss this case. He thought, as Dr. Richardson did, that the probable diagnosis was carcinoma of the head of the pancreas and that the patient deserved exploration. This was carried out and the enlarged gall bladder contained rather light colored bile and quite a bit of gravel-like sediment. The common duct was dilated. An attempt to pass a probe through the ampulla was fruitless, and the surgeon had the impression that with the tip of the probe he could feel a soft tumor mass rather than a stone. Since he was unable to decide from above, he opened the duodenum in order to palpate the ampulla from both sides. On doing that he became convinced that there was a tumor in the ampulla.



He could not make out any extension, and it seemed that it might be possible to resect it. It was not believed, however, that the patient could stand the operation at that time. So the gall bladder was drained and the patient was sent home for a few weeks, to return to the hospital for radical resection. At that time the pyloric antrum of the stomach, the first and second portions of the duodenum and half of the pancreas were resected. The remaining pancreas was sutured into the intestinal wall, and the operative reconstructions were carried out. After a stormy convalescence she was able to leave the hospital in fairly good shape.

The resected specimen showed a small tumor — only about 2 cm in diameter — sharply restricted to the region of the ampulla but extending a little way up the common bile duct and a little way up the pancreatic duct. The mouths of both the bile duct and the pancreatic duct were found in the small ulcerated crater of the tumor. Microscopic examination showed a fairly well differentiated adenocarcinoma. There were numerous enlarged regional lymph nodes, but all of them were free from metastases, and so far as one could judge, the tumor seemed to have been completely removed.

DR RICHARDSON: Did they biopsy the liver?

DR MALLORY: No biopsy specimen was taken. The liver was smooth and moderately bile stained. They thought that it was normal except for the bile stasis, and at the time of the second operation most of that had disappeared.

A PHYSICIAN: Where did you say that the tumor arose?

DR MALLORY: It was a carcinoma of the ampulla of Vater. There are both benign papillomas and malignant carcinomas of the ampulla. I am not sure that in this hospital we have ever seen a benign papilloma, but there are numerous cases on record. One other point worth remembering when the question of operation arises is that it is quite possible to find a benign as well as a malignant neoplastic obstruction, if the patient can be suitably prepared for operation, it is well worth the risk to attempt resection.

## CASE 32142

### PRESENTATION OF CASE

*First admission* A thirty-four-year-old Irishman entered the hospital because of severe pain in the epigastrium and left flank of four days' duration.

Five years before entry he first began to suffer from gnawing, burning nonradiating pain in the epigastrium following meals by one or two hours and usually relieved by food or sodium bicarbonate. These attacks had been cyclic in nature, with two-month to three-month periods of postprandial pain alternating with four-month to five-month periods of freedom from symptoms. Prior to entry he had had severe postprandial epigastric distress for three

weeks, gradually becoming worse and only partially relieved by food and alkali. On two occasions he vomited recently ingested food without gross blood. In addition to the epigastric distress he developed pain in the left groin that radiated to the flank and back.

Physical examination was negative except for a soft apical systolic murmur. The blood pressure was 140 systolic, 85 diastolic. The laboratory studies were essentially negative. A barium meal disclosed a constantly irregular duodenal cap with a fleck of barium in its lower portion.

After three weeks in the hospital the patient was discharged to be followed in the Out Patient Department.

*Second admission* (thirteen years later) During the interval the patient continued to have epigastric pain but refused to follow the dietary regimen described. He was, however, able to continue his work. The morning of re-admission he left home for work feeling well, but suddenly he was doubled up by an excruciating midline stabbing abdominal pain that spread to the umbilicus. This pain remained constant.

On physical examination the patient was a well developed and well nourished pale perspiring man in acute abdominal distress. The neck and chest were negative. The abdomen was tense with generalized spasm, most marked in the epigastrium. There was generalized tenderness, peristalsis was absent.

The temperature was 99°F, the pulse 112, and the respirations 40. The blood pressure was 170 systolic, 90 diastolic.

The white-cell count was 14,000, with 87 per cent neutrophils. The urine was normal.

The patient was taken to the operating room, and abdominal exploration was done. The duodenum was found to be heavily scarred, and there was a perforated duodenal ulcer, which was closed by sutures.

After the operation the patient was improved but continued to have epigastric pain and to run a temperature of 100°F. Two days later his condition suddenly became worse. He complained of severe, constant epigastric pain that occasionally radiated into the right groin. There was no vomiting. Morphine failed to bring relief. The blood pressure was 150 systolic, 90 diastolic. The abdomen was board-like, with tenderness and rebound pain, peristalsis was absent. He was prepared for operation, but after induction of anesthesia, his color suddenly became poor, his respirations shallow, and his pulse imperceptible. Despite all resuscitatory measures the patient went downhill rapidly and died.

### DIFFERENTIAL DIAGNOSIS

DR HOWARD ULFELDER: This patient, in brief, was a man of forty-seven with duodenal ulcer of

eighteen years' standing. No other organic lesion is described, nor does the history suggest that any was suspected.

The last admission was precipitated by perforation into the free peritoneal cavity. This was treated in orthodox surgical fashion, but the immediate postoperative course was marred by persistent fever and epigastric pain. On the second day there was a sharp turn for the worse. This complication was obviously considered amenable to surgical correction, but with the induction of anesthesia the patient took another sharp downward turn and soon expired.

Could this have been a pure anesthetic death? If so, one must still speculate on the nature of the complication that necessitated return to the operating room. It appears more plausible to me to assume that the burden of anesthesia alone was more than this patient could stand, his compensatory mechanisms had already been called on, and his reserves were spent. This view is supported by the fact that anesthesia precipitated a state of profound circulatory collapse. Although the possibility of asphyxia secondary to laryngospasm or aspirated gastric contents should be mentioned, the account of this man's terminal moments does not fit this diagnosis.

Turning now to the mishap that occurred on the second postoperative day, one can suspect that it was due either to a vascular accident or to peritonitis. The past history gives me no leads, although there is mention of pain in the left groin and flank at the time of the first hospital admission and in the right groin on the day of death. The former I shall ascribe to an unusual but not unheard of radiation from the upper gastrointestinal tract. The latter is easily explained by the presence of irritating or infected fluid in the right gutter.

Among vascular accidents, only mesenteric thrombosis deserves attention. Some evidence of obstruction usually accompanies this lesion. None is described here. Coronary occlusion, dissecting aneurysm and pulmonary embolism fail to fit either the symptoms or the physical findings.

Under the heading of peritonitis, mention must be made of a perforated gall bladder, appendix and bowel and of acute pancreatitis. None of these can be completely excluded, but all appear extremely unlikely.

Three lesions remain for serious consideration. Leakage at the site of the recent duodenal suture appears the likeliest, but according to the literature this is extremely rare. Rupture of a previously localized abscess would not be expected so soon after the primary insult. My diagnosis is perforation of a separate peptic ulcer. This also is infrequent,

but ulcers are notoriously multiple during periods of activity and one example of this coincidence was noted in a review of 334 cases of benign perforated ulcer observed in this hospital.\*

I predict, therefore, that post-mortem examination revealed early generalized peritonitis, recent duodenal perforation with intact closure, and a separate ulcer (probably gastric), with perforation into the free peritoneal cavity.

**DR RODOLFO E. HERRERA** When the patient was taken to the operating room the second time, it was our feeling that we were compelled to rule out a leak from the site of the previous perforation or from a new site. Although the patient had complained of pain almost constantly after recovery from his first anesthesia, his condition appeared good, there was, however, a definite exacerbation of pain on the second postoperative day. At that time an abdominal tap yielded coffee-grounds material grossly identical to that obtained through the Levine tube.

#### CLINICAL DIAGNOSIS

Perforated gastric ulcer

#### DR ULFELDER'S DIAGNOSES

Duodenal ulcer, repaired

Perforated gastric ulcer

Generalized peritonitis

#### ANATOMICAL DIAGNOSIS

Multiple perforated peptic ulcers of duodenum.

#### PATHOLOGICAL DISCUSSION

**DR HERRERA** At the time of the second laparotomy the ulcer on the anterior duodenal wall was found to be closed over adequately by an omental tab. On the posterior wall, just proximal to the pylorus, a second perforation was found, this measured at least 7 mm in diameter, and through it gastric contents poured out freely. At that point in the operation the patient was no longer breathing and his heart had stopped. We found it impossible to tell how old the second perforation was, in other words, we were not certain whether this man had perforated the second ulcer on the second postoperative day or whether two perforations had been present at the time of the first operation.

**DR TRACY B. MALLORY** Dr Herrera's description of the findings at the second operation appears to explain adequately the terminal episode. Permission for post-mortem examination was refused.

\*Ulfelder II, and Allen A W. Acute perforation of ulcers of stomach and duodenum. *New Eng J Med* 227:780-784 1942

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## PEDIATRIC SURVEY

COMPLACENCE is the natural enemy of progress but, fortunately, satisfaction with any level of achievement, if too long indulged, is usually shattered by forces from without, coming to demand a higher grade of production in favor of the consumer. Medicine in this country has not ordinarily needed such stimulation for it has felt the necessity of meeting new challenges, and pediatrics, no less than other branches of medicine, has so far always found ahead of it new standards on which to form its line.

Pediatrics, spurred on perhaps by political rumblings that suggest a storm on the horizon, has now initiated its own psychoanalytical survey, with the American Academy of Pediatrics in the role of

analyst, it has found wisdom in the Socratic injunction to know thyself.

This study of child-health services has already been conducted during the past year in North Carolina as a pilot state, and similar country-wide state programs are about to be launched. A steering committee has been appointed within the American Academy of Pediatrics representing the Academy, the American Pediatric Society and the Medical Advisory Board of the Children's Bureau. Dr. John P. Hubbard, of Boston, has accepted the position as director of the study.

The inquiries to be made will cover four major fields: pediatric education, distribution, qualification and activities of professional personnel, hospital and clinic facilities, and general health services. The study in Massachusetts, soon to be initiated, will be directed by Dr. Lendon Snedeker, of Boston; it has been approved by the Council of the Massachusetts Medical Society.

The work of gathering data will fall on the pediatricians of the state who will be asked to fill out questionnaires concerning their own activities and assist in obtaining information from physicians in private practice and from hospitals. They will also be asked to help publicize the program through newspapers, radio broadcasts and group meetings.

Such a program suggests that the pediatricians of the country intend to do a thorough job in finding out what type of care is being given to our children by hospitals, health services, the general practitioners and themselves. It is hoped that the study will determine, so far as possible, what quality as well as what type of service is delivered, in what proportions pediatric practice is conducted for the benefit of the patient and of the doctor, and what the true standards of service should be.

The evaluation of present methods of child care and the establishment, where necessary, of better ones are undertakings that warrant general support.

## DANGERS OF CHEMOPROPHYLAXIS

IN THE past few years, a number of papers have appeared indicating that prolonged and continuous administration of sulfanilamide or sulfadiazine in small doses may be used effectively as a prophy-

lactic against hemolytic streptococcus infections. At first, the writers were concerned primarily with the prevention of recrudescences of rheumatic fever, and the data that they present suggest that such recrudescences were significantly reduced in susceptible individuals, as compared with controls in whom such prophylaxis was not used. Some subjects had to be eliminated from the treated groups because of toxic reactions, which sometimes were quite serious. The types of patients chosen, however, were such that considerable risks were warranted since hemolytic streptococcus infections in them would frequently have been followed by serious rheumatic activity resulting in crippling and even fatal cardiac involvement.<sup>1-5</sup>

It is interesting that positive throat cultures for hemolytic streptococci were not eliminated or prevented and that their incidences were not appreciably reduced among the recipients of this form of prophylaxis. Furthermore, in studies on cases of hemolytic streptococcus tonsillitis and pharyngitis in which therapeutic doses of sulfadiazine had been used, the incidence of Group A hemolytic streptococci in throat cultures was found to be reduced only during the period of treatment, after treatment was stopped, positive cultures were found just as frequently in patients who had been treated with the full doses continuously for three to seven days as they were in comparable untreated cases.<sup>6-9</sup>

The possibility of developing sulfonamide-resistant strains of pathogenic organisms during treatment with doses of drug that are ineffective for the complete elimination of the infecting organism is a serious and important consideration in the prophylactic use of chemotherapeutic and antibiotic agents. In vitro and in experimental infections in animals such resistance can be readily produced in many organisms by prolonged exposure to subeffective concentrations of these therapeutic agents. Whether this is a process of selection whereby the resistant variants survive or whether it is due to a change in the metabolism of the organism — a sort of acclimatization — is not entirely clear. It is evident, however, that the less susceptible the organism is in the first place, the easier it is to enhance its resistance. Furthermore, it is reasonable to suppose that the extensive and prolonged use of drugs in

subeffective amounts carries with it the greatest danger of the development and spread of resistant strains, irrespective of the mechanism whereby the organisms become resistant. Attention has been called in these columns on previous occasions both to the dangers of the continuous use of sulfonamides to the patient<sup>10</sup> and to the possibility of the development and spread of resistant strains.<sup>11</sup> These dangers and the responsibilities of the physician and patient with respect to sulfonamide prophylaxis and treatment have been ably reviewed by Morgan and Turner.<sup>12</sup>

Two types of mass prophylaxis with sulfadiazine have been employed in military establishments. One of these was a brief course, varying from a single dose to several doses given over a period of one or two days, for the purpose of preventing and eliminating meningococcal infections.<sup>13-15</sup> The other was a continuous administration of small doses of sulfadiazine over several weeks, given primarily for the purpose of preventing hemolytic streptococcus diseases.<sup>16-18</sup> The former resulted in immediate and almost complete elimination both of infections and of carriers until the organisms were gradually introduced again from outside. The latter produced a reduction in manifest streptococcal diseases without eliminating the organisms from carriers or preventing their spread. These results could have been anticipated from the extreme sensitivity of the meningococcus to sulfadiazine on the one hand and the resistance of the hemolytic streptococci on the other. Resistance or fastness of meningococci to sulfadiazine is produced with the greatest difficulty even in vitro, whereas it is readily produced in streptococci. Other factors concerned with the host-parasite relation may also be of equal or greater importance with respect to these two organisms, but they are difficult to evaluate. At any rate, the anticipated effect of the continued use of sulfadiazine in small doses in a population heavily infected with virulent streptococci finally materialized. Resistant strains of hemolytic streptococci spread throughout several of the units where sulfadiazine prophylaxis was being carried out. These resistant strains essentially replaced susceptible strains and gave rise to rather extensive outbreaks of hemolytic streptococcus infections.

Two reports of such a sequence of events in different Navy training stations have recently been reported,<sup>19, 20</sup> and others have undoubtedly occurred. It is difficult to tell without a considerably greater amount of information than has been made available thus far whether the widespread prophylactic program adopted by the Navy had the total effect on the training program that was anticipated by the medical authorities. Data, likewise, are lacking from which one can estimate just how much harm was done in misdiagnosed or improperly treated cases as a result of sensitization or from other toxic effects that resulted directly or indirectly from this prophylactic regime. It is clear from these experiences, however, that sulfonamide prophylaxis on a large scale and over a long period carries with it considerable possibilities of harm, which must always be weighed against the anticipated benefits.

No doubt the availability of penicillin in large quantities, particularly in the form of troches and oral preparations, has suggested to many physicians the possibility of its continuous use in the prophylaxis of various types of infections. Although fewer and perhaps less serious toxic effects may be expected from penicillin than from the sulfonamides, the possibilities for harm should be explored under rigidly controlled conditions before any such programs are undertaken.

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## MASSACHUSETTS MEDICAL SOCIETY REVIEW LECTURE COURSE

The following is a detailed program of the balance of the Review Lecture Course, which concludes on May 15

APRIL 17 ALLERGY *Chairmen* John L. Fromer and Francis M. Rackemann

3 00-4 45 Round-Table Discussion on Hay Fever and Asthma. Walter Burrage assistant physician, Massachusetts General Hospital. Calvin B. Faunce consulting surgeon, Massachusetts Eye and Ear Infirmary. John L. Fromer director, Department of Allergy and Dermatology, Lahey Clinic. J. Everts Greene assistant in medicine, Massachusetts General Hospital. Sanford B. Hooker professor of immunology, Boston University School of Medicine. Francis M. Rackemann lecturer in medicine, Harvard Medical School, physician, Massachusetts General Hospital. Leroy E. Schall professor of laryngology, Harvard Medical School, chief, Department of Otolaryngology, Massachusetts Eye and Ear Infirmary.

NOSE AND THROAT DISEASES *Chairmen* Calvin B. Faunce and Leroy E. Schall

4 45-5 30 DEAFNESS AND WHAT CAN BE DONE ABOUT IT. Moses H. Lurie assistant professor of otology, Harvard Medical School, surgeon in otology, Massachusetts Eye and Ear Infirmary, consulting otolaryngologist, Massachusetts General Hospital.

5 30-6 00 Emergencies Involving the Nose, Throat and Bronchi. John R. Richardson instructor in laryngology, Harvard Medical School, assistant surgeon, Massachusetts Eye and Ear Infirmary, assistant surgeon, Massachusetts General Hospital.

APRIL 22 DISEASES OF THE CHEST *Chairmen* Donald S. King and John W. Strieder

5 00-5 30 Public-Health Aspects of Tuberculosis in Massachusetts. Alton S. Pope deputy commissioner and director of the Division of Tuberculosis, Massachusetts Department of Public Health.

5 30-6 00 The Present Concept of the Treatment of Pulmonary Tuberculosis. Paul Dufault superintendent, Rutland State Sanatorium.

6 00-6 30 Important Points to Remember in Treating Lung Conditions. Theodore L. Badger chief-of-staff, Channing Home, instructor in medicine, Harvard Medical School.

7 30-8 15 Pulmonary Carcinoma and Other Growths in the Chest. Ralph H. Adams surgeon, Lahey Clinic.

8 15-9 00 Pulmonary Abscess, Bronchiectasis and Other Suppurative Chest Conditions. Richard H. Sweet associate visiting surgeon, Massachusetts General Hospital, instructor in surgery, Harvard Medical School.

APRIL 24 NEUROPSYCHIATRY *Chairmen* Raymond D. Adams and Harry C. Solomon

3 00-3 35 Psychosomatic Medicine. Stanley Cobb psychiatrist-in-chief, Massachusetts General Hospital.

3 35-4 05 Psychoneurosis and the Veteran. John Murray, consultant in psychiatry, Massachusetts Institute of Technology.

4 05-4 40 Insulin-Shock and Electric-Shock Therapy and Lobotomy Gaylord P Coon medical officer, Boston Psychopathic Hospital, junior associate, Peter Bent Brigham Hospital

4 40-5 20 Neurosyphilis Augustus S Rose member of staff, Psychopathic Hospital, consultant, Massachusetts General, Peter Bent Brigham, New England Baptist and Newton hospitals

5 20-6 00 Epilepsy William G Lennox visiting physician, Children's Hospital, visiting neurologist, Boston City Hospital, assistant in neurology, Peter Bent Brigham Hospital

#### APRIL 29 NEUROPSYCHIATRY (Continued)

5 00-5 30 Headache Derek Denny-Brown professor of neurology, Harvard Medical School, director, Neurological Unit, Boston City Hospital

5 30-6 00 Pyogenic Intracranial Infections Charles S Kubik neurologist and neuropathologist, Massachusetts General Hospital

6 00-6 30 Apoplexy Raymond D Adams visiting neurologist and neuropathologist and assistant director, Neurological Unit, Boston City Hospital, consultant in neurology, Pratt Diagnostic Hospital, lecturer in neurology, Tufts College Medical School

#### APRIL 29 ENDOCRINOLOGY Chairmen Edwin B Astwood and Lewis M Hurxthal

7 30-8 15 Progress in Endocrinology and Thiouracil in the Treatment of Hyperthyroidism Edwin B Astwood research professor of medicine, Tufts College Medical School

8 15-9 00 Diagnosis and Treatment of Thyroid Disease Frank H Lahey director, Lahey Clinic, surgeon-in-chief, New England Baptist and Deaconess hospitals

#### MAY 1 ENDOCRINOLOGY Chairmen Edwin B Astwood and Lewis M Hurxthal

3 00-3 30 Childhood Obesity and Related Problems Richard Wagner assistant professor of pediatrics, Tufts College Medical School, physician, Boston Floating Hospital

3 30-4 00 Hypothyroidism and Hypopituitarism Lewis M Hurxthal director, Department of Medicine, Lahey Clinic, physician, New England Baptist and Deaconess hospitals

4 00-4 30 Treatment of Addison's Disease George W Thorn Hersey Professor of the Theory and Practice of Physic, Harvard Medical School, physician-in-chief, Peter Bent Brigham Hospital

4 30-5 15 Hyperparathyroidism Oliver Cope assistant professor of surgery, Harvard Medical School, associate visiting surgeon, Massachusetts General Hospital

5 15-6 00 Male Hypogonadism and the Therapeutic Use of Androgens Robert W Williams associate in medicine, Harvard Medical School, junior visiting physician and assistant, Thorndike Memorial Hospital, Boston City Hospital

#### MAY 6 DISEASES OF THE EYE Chairmen Edwin B Dunphy and Benjamin Sachs

5 00-6 00 Ophthalmology in General Practice Benjamin Sachs professor of ophthalmology, Tufts College Medical School Edwin B Dunphy chief of ophthalmology, Massachusetts Eye and Ear Infirmary

#### DIABETES MELLITUS Chairmen W Richard Ohler and Howard F Root

6 00-6 30 Diagnostic Methods Priscilla White instructor in pediatrics, Tufts College Medical School, physician, New England Deaconess Hospital

Dietary Treatment Joseph Rosenthal assistant professor of medicine, Tufts College Medical School, supervisor in charge of teaching, Boston Dispensary

7 30-9 00

The Insulins George Ballantyne director, Diabetic Clinic, Worcester City Hospital

Complications James Townsend associate physician, Massachusetts General Hospital

Acidosis and Coma Howard F Root associate in medicine, Harvard Medical School, physician-in-chief, New England Deaconess Hospital

Advances in Diabetes Elliott P Joslin clinical professor of medicine (emeritus), Harvard Medical School, medical director, George F Baker Clinic, New England Deaconess Hospital

#### MAY 8 GYNECOLOGY Chairmen Joe V Meigs and John Rock

3 00-3 45 Menstruation, Its Disorders and Their Treatment John Rock instructor in gynecology, Harvard Medical School, visiting surgeon, Free Hospital for Women

3 45-4 30 Office Problems, Diagnostic Methods and Treatment James C Janney professor of gynecology, Boston University School of Medicine

4 30-5 15 Diagnosis of Cancer Joe V Meigs clinical professor of gynecology, Harvard Medical School, chief, Vincent Memorial Hospital and Gynecological Service, Massachusetts General Hospital

5 15-6 00 Treatment of Cancer George Van S Smith visiting surgeon and director of the Fearing Research Laboratory, Free Hospital for Women

#### MAY 13 OBSTETRICS Chairmen Alonzo K Paine and Duncan E Reid

5 00-6 30 and 7 30-9 00 A Critical Review of Progress in Obstetrics During the Last Four Years, including a Consideration of Certain Immediate Problems of the Newborn Roy J Heffernan visiting obstetrician and gynecologist, Carney Hospital Harold H Rosenfield visiting surgeon in obstetrics and gynecology, Boston City Hospital Stewart H Clifford pediatrician, Boston Lying-in Hospital associate visiting physician, Children's Hospital Arthur T Hertig pathologist and obstetrician to Out-Patient Department, Boston Lying-in Hospital

#### MAY 15 SURGICAL GENITOURINARY DISEASES AND VENEREAL DISEASES Chairmen Roger C Graves and Samuel N Vose

3 00-3 40 Prostatism George G Smith visiting urologist, Massachusetts General Hospital, urologist, Palmer Memorial Hospital

3 40-4 25 The Female Bladder Samuel N Vose professor of genitourinary surgery, Boston University School of Medicine, urologist, Massachusetts Memorial Hospitals

4 25-5 00 Epidemiology of Venereal Disease Erwin C Drescher surgeon, United States Public Health Service

5 00-5 30 Recent Advances in the Management of Gonorrhea in the Male J Hartwell Harrison urological surgeon, Peter Bent Brigham Hospital

5 30-6 00 Progress in the Diagnosis and Treatment of Syphilis John G Downing professor of dermatology and syphilology, Tufts College Medical School, professor of dermatology, Boston University School of Medicine, dermatologist-in-chief, Massachusetts Memorial, Boston City and St Elizabeth's hospitals

## CORRESPONDENCE

### DEPRIVATION OF LICENSE

To the Editor At a meeting of the Board of Registration in Medicine held March 15, the Board took the following actions

To suspend the registration of Dr Edmond J MacDonald, 24 Wheatland Street, Somerville, for six months because of gross misconduct in the practice of his profession as shown by his treatment of patients

To revoke the registration of Dr Earl Burton Carr of Cassadago, New York, and Bar Harbor, Maine, because of gross misconduct in the practice of his profession as shown by his conviction of a felony in New York State

H QUIMBY GALLUPE, M D, Secretary,  
Board of Registration in Medicine

State House  
Boston

(Notices on page xix)

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## ALTERNATING PLEURISY WITH EFFUSION AS A MANIFESTATION OF TUBERCULOSIS\*

### A Report of Seven Cases

KENNETH T. BIRD, M.D.†

WALTHAM, MASSACHUSETTS

THE syndrome of alternating pleurisy with effusion is characterized by the development of serofibrinous pleurisy, at first unilateral and later contralateral. The onset and course of each effusion associated with this syndrome differ in no way from that of the more frequent purely unilateral type of pleurisy. Occurring as it does in the absence of pulmonary infiltration or with only a suspicion of it, this condition presents a diagnostic, therapeutic and prognostic challenge.

This syndrome has received scant clinical attention, and only isolated case reports have appeared. Gray<sup>1</sup> describes alternating pleurisy with effusion in an eighteen-year-old boy, with death resulting from military tuberculosis and tuberculous meningitis. Hurrell and Dawson-Walker<sup>2</sup> report a single case of alternating pleurisy with effusion occurring in a twenty-six-year-old man. Autopsy revealed generalized military tuberculosis. Gordon<sup>3</sup> briefly cites a case seen by Theodos of alternating pleural effusion with subsequent ascites developing in the presence of Pott's disease of the spine.

Hitherto, alternating pleurisy with effusion has been termed "bilateral pleurisy with effusion." It seems desirable to reserve the latter term for the rare cases of acute simultaneous bilateral pleurisy with effusion, thus demarcating the definite syndrome of alternating pleurisy with effusion.

Wilson<sup>4</sup> has summarized 14 cases of bilateral pleurisy with effusion. Of these, only 3 developed in the absence of demonstrable pulmonary infiltration and thus seemingly fall into the category under discussion, but it is not clear whether these cases represent alternating pleurisy with effusion or acute simultaneous bilateral pleurisy with effusion. It is probable that most cases of acute bilateral pleurisy with effusion actually represent alternating pleurisy with effusion, first discovered when bilateral effusion was present.

Cases of alternating pleurisy with effusion with definite evidence of widespread pulmonary tuberculosis are not included in the syndrome of alternating

pleurisy with effusion, because the diagnosis is usually obvious. Effusions occurring during the course of bilateral therapeutic pneumothorax likewise are not considered, nor are the occasional cases of contralateral effusion developing after a unilateral artificial pneumothorax, with an accompanying effusion.

Acute serofibrinous pleurisy is of tuberculous origin in many, if not all, cases. Numerous follow-up studies, recently summarized by Farber,<sup>5</sup> attest to the serious ultimate prognosis of so-called serofibrinous pleurisy, an apparently benign and transient disease. Thirty to fifty per cent of cases of pleurisy with effusion later develop pulmonary tuberculosis. Occasionally military tuberculosis follows or accompanies such an effusion, and extrapulmonary tuberculosis is not infrequently a complication.

That alternating pleural effusion may be a manifestation of tuberculosis is shown by the following cases seen at the Middlesex County Sanatorium.

### CASE REPORTS (FIGS 1 and 2)

**CASE 1.** H. S. (M.C.S. 2155), a 30-year-old, married housewife, a sextigravida, when in the 5th month of pregnancy developed left-sided pleurisy and was hospitalized elsewhere on March 11, 1939, for 7 days. A roentgenogram of the chest showed a marked left-sided pleural effusion. A diagnostic thoracentesis was performed, and the fluid obtained was reported as positive for tuberculosis by guinea-pig inoculation. Because of recurrence of left-sided chest pain, the patient was readmitted elsewhere on March 29. A roentgenogram again showed a marked left-sided effusion. Following thoracentesis and further symptomatic treatment, she was discharged on April 12, somewhat improved.

The patient was first seen at the Diagnostic Clinic of the Middlesex County Sanatorium on April 24. A chest roentgenogram still showed a left-sided pleural effusion with cardiac displacement. Because she was in the 6th month of pregnancy, bed rest at home was advised. On July 30, acute right-sided pleuritic pain developed and she was again hospitalized elsewhere. A right-sided pleural effusion was present. On August 1, she delivered a normal baby, who died 1 week later.

The patient was admitted to this hospital on August 14 with a slight cough, minimal expectoration and a temperature of 103°F. A roentgenogram of the chest showed a right-sided pleural effusion, with slight haziness only at the left costophrenic angle. A right-sided thoracentesis performed on August 18 produced hazy amber fluid, which was positive for tuberculosis by guinea-pig inoculation. There was progressive improvement, and a roentgenogram taken on No-

\*From the Middlesex County Sanatorium.

†Formerly resident in tuberculosis, Middlesex County Sanatorium, and instructor, Department of Preventive Medicine, Tufts College Medical School, Boston.

September 15 showed only a small amount of fluid at the right base. The patient was discharged on March 16, 1940, after 216 days of residence.

When last seen on April 2, 1945, she was essentially well. A roentgenogram of the chest showed increased markings at the right base. Both costophrenic angles appeared normal.

*Comment* There was an acute onset of left-sided pleural effusion, with fluid positive for tuberculosis by guinea-pig inoculation, in the 5th month of pregnancy. This was fol-

The patient remained essentially well until February 9, 1945, when he developed acute malaise, chills and fever and rapidly became disoriented. A diagnosis of bronchopneumonia with left-sided pleural effusion was made by his physician after a chest roentgenogram, and he was admitted elsewhere. The sputum was negative for tubercle bacilli. Oral sulfadiazine and later intramuscular penicillin in adequate dosage were given, without apparent benefit. A left-sided thoracentesis was first done on February 28. No organisms

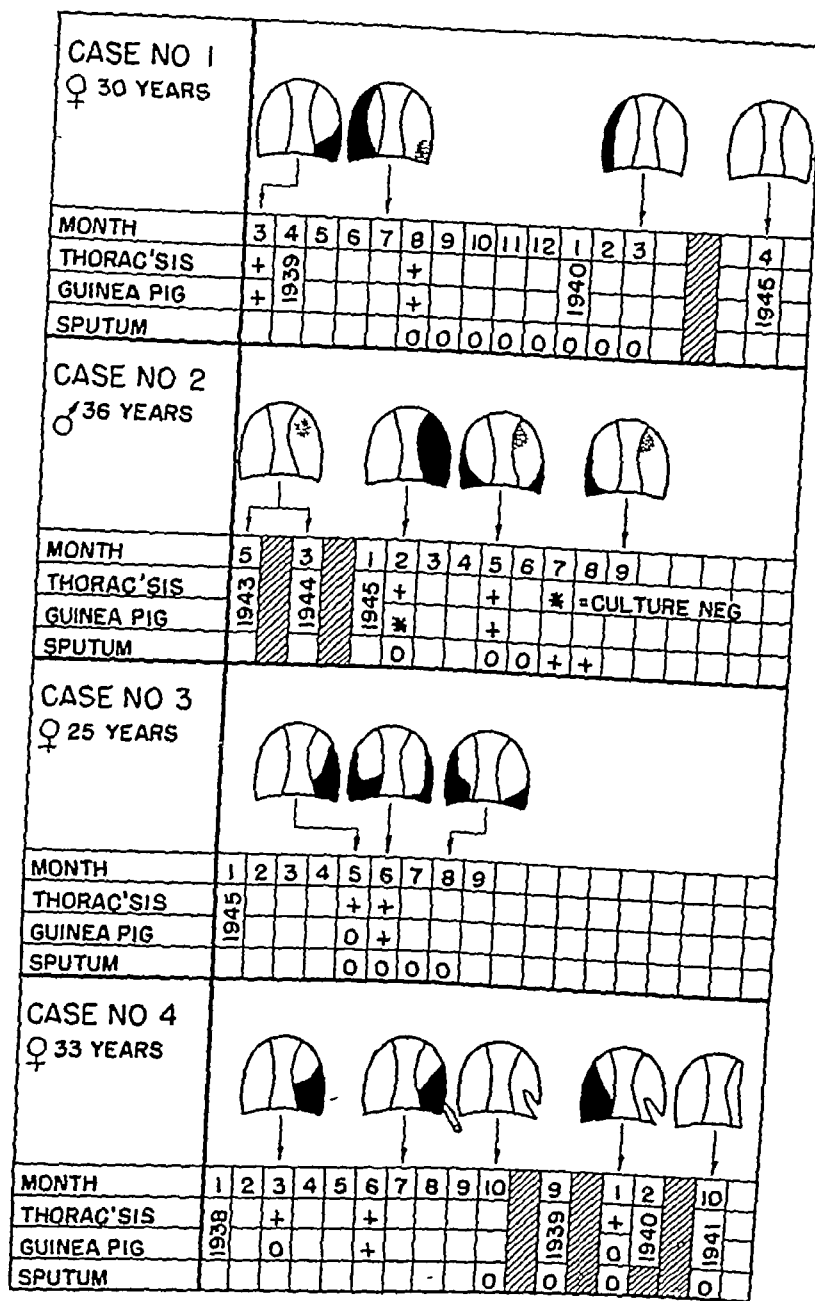


FIGURE 1

lowed 4½ months later by acute right-sided pleural effusion, with the fluid again positive

CASE 2 C F (MCS 3931), a 33-year-old pipefitter's helper, was first seen in the Diagnostic Clinic on May 24, 1943, as a draft rejectee, when a chest roentgenogram showed questionable infiltration in the 1st left interspace and he was classified as a tuberculous suspect. Roentgenograms taken on August 25 and on March 8, 1944, showed no change.

were isolated, and after 8 weeks of culture no tubercle bacilli were obtained. Following a second thoracentesis in the middle of March, a tube was inserted for drainage and penicillin irrigations were done. There was gradual improvement, and on April 18 a chest roentgenogram showed almost complete disappearance of the effusion, with infiltration in the left left interspace. The right lung was clear. On May 5, the patient was discharged pending admission to this hospital. On admission on May 17, 1945, a chest roentgenogram showed on the right a moderate pleural effusion and on the



left definite minimal infiltration in the 1st interspace, with thickened pleura at the base. No symptoms were associated with the appearance of this effusion. A right-sided thoracentesis performed on May 22 yielded 300 cc. of blood-tinged fluid, which was positive for tuberculosis by guinea-pig inoculation. On May 29, the fasting gastric content was negative for tuberculosis by guinea-pig inoculation, but routine 72-hour sputum concentrates on July 5 and August 14 were both positive for tubercle bacilli (Gaffky II) on a Ziehl-Neelsen smear. The patient is still hospitalized.

*Comment* There was an acute onset of left-sided effusion, with a negative culture, followed by asymptomatic right-sided effusion, with the fluid positive by guinea-pig inoculation, in the presence of definite minimal left-sided infiltration that was previously only suspected. The interval between effusions was 3 months. The sputum eventually became positive.

**CASE 3 D W (MCS 3927)**, a 25-year-old, unmarried Chinese woman developed a cough in February, 1945, which was diagnosed as bronchitis. On March 2, there developed slight pain in the thorax and acute diffuse abdominal swelling.

The patient was admitted to this hospital on May 16, with moderate ascites and a small left-sided pleural effusion without parenchymal disease. A tuberculin test (0.01 mg.) was positive. The past history revealed that on May 12, 1943, because of vague abdominal complaints, laparotomy had been performed elsewhere. Considerable induration of the lower ileum was found. An appendectomy was performed, with removal of a cyst of the left ovary and of the left fallopian tube. Tuberculous peritonitis was considered but not proved. The pathological diagnoses were endometrial cyst of the ovary, chronic pyelonephritis and questionable chronic appendicitis.

Clear, straw-colored fluid obtained by a left-sided thoracentesis on May 22 was negative for tuberculosis by guinea-pig inoculation. The aspirated gastric content on May 24 was negative for tuberculosis on guinea-pig inoculation. Specimens of the sputum were negative on concentration.

In early June, while the patient was still hospitalized, a slight cough, right-sided chest pain, dyspnea and a temperature of 100°F developed. On June 9 a chest roentgenogram showed a massive right-sided pleural effusion, with considerable absorption of fluid on the left. Four hundred cubic centimeters of thin, slightly cloudy, straw-colored fluid obtained by thoracentesis on June 12 was positive for tuberculosis by guinea-pig inoculation. By June 19 there was no evidence of ascites. Despite further aspiration in an attempt to prevent fixation, a right-sided fibrothorax has developed, with marked limitation of right hemithoracic movement. The patient is still hospitalized.

*Comment* The insidious onset of left-sided pleural effusion, with the fluid negative by guinea-pig inoculation, was coincidental with transient ascites, followed by the gradual onset of right-sided effusion, with the fluid positive. The interval between effusions was 3 months. Previous laparotomy suggested tuberculous peritonitis. There was eventual development of right-sided fibrothorax.

**CASE 4 M O (MCS 2275)**, a 33-year-old, married housewife, developed a slight cough with pain in the left posterior chest in January, 1938, when 1 month pregnant. In March, malaise increased, slight fever began, and a heavy feeling developed in the left side of the chest. A roentgenogram taken on March 30 showed a left-sided pleural effusion. A left-sided thoracentesis performed elsewhere on March 31 yielded 480 cc. of fluid, which was negative for tuberculosis by guinea-pig inoculation. On May 29, vaginal bleeding began, and on June 2, incomplete miscarriage occurred. Curettage was done elsewhere on June 4, and convalescence was normal until June 17, when the temperature rose to 103°F and a septic course developed. On June 25, a left-sided diagnostic thoracentesis yielded fluid that was positive for tuberculosis by guinea-pig inoculation. On July 6, the patient was transferred to another hospital, where a left-sided thoracentesis yielded fluid containing anaerobic nonhemolytic streptococci. On July 9, rib resection for tube drainage was done. A pleural biopsy showed tuberculous granulation tissue.

The patient was transferred to this hospital on July 29 with a diagnosis of mixed tuberculous and nonhemolytic streptococcus empyema, with no evidence of parenchymal disease, but left against advice on the 13th day.

Irrigation of the draining empyema cavity was done at home until September, when the temperature rose to 104°F and the patient was hospitalized elsewhere. A secondary hemolytic streptococcus infection of the empyema cavity was found. The cavity had decreased in volume from about 200 cc. to 120 cc.

The patient was readmitted to this hospital on October 6. Empyema fluid was positive for tuberculosis by guinea-pig inoculation and also showed diphtheroids, streptococci and staphylococci. Frequent irrigations of the empyema cavity resulted in slow improvement. On February 14, 1939, a left-sided Schede thoracoplasty, with partial removal of the 6th, 7th, 8th, 9th and 10th ribs was done, but the incision broke down postoperatively. No further interference was advised because of the patient's condition, and she was discharged on September 21 after 351 days of residence.

Wound irrigations were continued at home. The patient remained fairly well until January, 1940, when she developed pain in the right side of the chest, cough, a temperature of 101°F, dyspnea and nausea. She was readmitted to this hospital on January 18 with a moderate right-sided pleural effusion. The left-sided thoracic incision was still open and draining. A right-sided thoracentesis on January 19 yielded 900 cc of thin, cloudy, amber fluid, with the specific gravity 1.025, the red-cell count 637, and the white-cell count 360, with 1 per cent polymorphonuclear leukocytes, 96 per cent lymphocytes, 2 per cent eosinophils and 1 per cent undetermined forms. The fluid was negative for tuberculosis by guinea-pig inoculation. By April 9 there was only slight blunting of the right costophrenic angle with fluid. A three-stage left anterolateral thoracoplasty was begun on April 10 and completed on May 15. The patient did well postoperatively, the new incision healed fully, and closure of the old draining wound began. The sputum was never positive. She was discharged on October 1, 1941, after 623 days of residence.

By April, 1944, the old wound was fully healed without drainage. When last seen on April 9, 1945 the patient was essentially well but on limited activity. A roentgenogram of the chest showed a left-sided thoracoplasty with excellent lateral compression. The right lung was clear, with a normal-appearing right costophrenic angle.

*Comment* There was an insidious onset of left-sided pleural effusion, with the fluid positive by guinea-pig inoculation, which after an incomplete miscarriage became secondarily infected and eventually required a left-sided Schede thoracoplasty. This was not successful and was followed by acute right-sided effusion, with the fluid negative by guinea-pig inoculation. The interval between effusions was 24 months. A left-sided thoracoplasty was required for final control. This catastrophic series of events could have undoubtedly been prevented by the present-day use of penicillin.<sup>4</sup>

**CASE 5 A. Z (MCS 2001)**, a 35-year-old, married housewife, with no known contact with tuberculosis, experienced the insidious onset of right-sided pleurisy in December, 1938. On January 8, 1939, she developed shaking chills and a temperature of 103°F. A roentgenogram of the chest taken elsewhere showed a right-sided pleural effusion from the 7th rib downward. A smear of the fluid showed no acid-fast organisms, 98 per cent of the cells were lymphocytes, and 2 per cent were polymorphonuclear leukocytes. Guinea-pig inoculation was not done. On February 15, when the patient was first seen in the Diagnostic Clinic, an attempted thoracentesis was unsuccessful.

The patient was admitted to this hospital on February 27, 1939. A 72-hour specimen of sputum taken on March 6, 1939, by the Greenfield-Anderson technic was positive for tubercle bacilli (Gaffky II), and stereoscopic roentgenograms on March 29 showed definite infiltration on the left, extending out from the upper pole of the hilum posteriorly to the 3rd rib and consistent with minimal pulmonary tuberculosis. This gradually retrogressed. Further sputum specimens remained negative. The patient was discharged on September 22 after 208 days of routine sanatorium care.

She remained well until November 19, when she developed acute left-sided chest pain, chills, a temperature of 102°F, cough and expectoration. Examination showed dullness to percussion with poor to absent breath sounds at the left base anteriorly and posteriorly. A chest roentgenogram taken on November 29 showed haziness at the extreme costophrenic angle on the right and a left-sided pleural effusion.

The patient refused readmission but took bed rest at home for 4 months. Thoracentesis was not done. By May, 1940, she was asymptomatic, and a roentgenogram showed only a small amount of fluid at the left base. In July, 1945, she was still well, and a roentgenogram showed the lungs to be clear and the costophrenic angles normal.

*Comment.* There was an acute onset of right-sided effusion and later transient left-sided infiltration, with a single sputum specimen positive. This was followed by acute left-sided effusion. The interval between effusions was 10 months.

**CASE 6** M<sup>r</sup>B (MCS 3502), a 36-year-old, divorced woman, was first seen in the Diagnostic Clinic on November 23, 1939, because of contact with her brother, who was under

chest pain. A massive left-sided pleural effusion with cardiac displacement was shown on examination and by chest roentgenogram.

The patient was readmitted on November 3, 1943. A left-sided thoracentesis yielded 600 cc. of Burgundy-red fluid, which was negative by guinea-pig inoculation. Fluid aspirated on November 12 and 27 was also negative. Sputum concentrates were consistently negative. Liver injections were begun, and the red-cell count rose from 3,430,000, with a hemoglobin of 78 per cent (Sahli), on admission to 4,000,000 on April 4, 1944, and to 4,850,000, with a hemoglobin of 88 per cent, on discharge. On March 7, the fasting gastric content was negative by guinea-pig inoculation. On

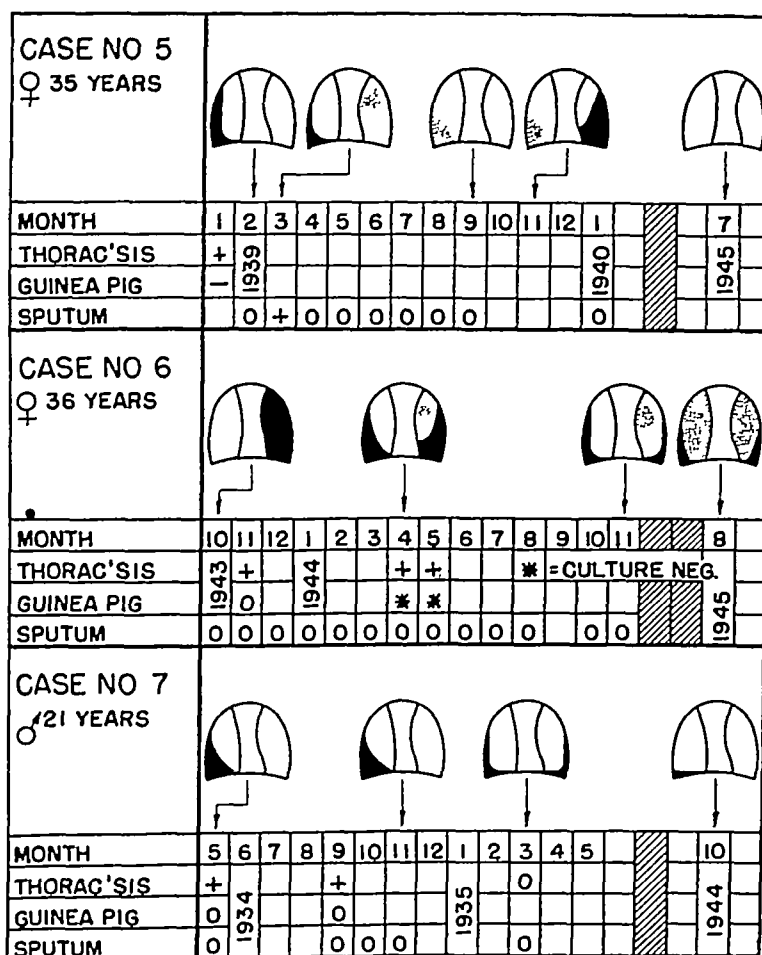


FIGURE 2

treatment for pulmonary tuberculosis. A chest roentgenogram was negative. Because of fatigue and weight loss, roentgenograms were taken elsewhere in September, 1941, and a diagnosis of tuberculosis was made.

On October 2, 1941, the patient was admitted to this hospital. A tuberculin test (0.01 mg.) was positive. A roentgenogram showed mixed infiltration on the left, extending from the hilum to the 2nd interspace. Seven 72-hour sputum concentrates, two gastric aspirations with guinea-pig inoculation and a sputum inoculated into a guinea pig were negative. The patient left the hospital against advice on December 26 after 86 days of residence. After discharge she was seen periodically in the clinic and remained free of respiratory complaints, but in November, 1942, a diagnosis of pernicious anemia (later confirmed) was made elsewhere and injections of liver extract were begun. In October, 1943, she developed an unproductive cough and a temperature of 102°F, without

routine sanatorium regimen the patient progressed satisfactorily until April 18, when severe cough, right-sided chest pain, shortness of breath and a temperature of 102°F developed coincidentally with a right-sided pleural effusion. A roentgenogram showed persistent effusion on the left and moderate effusion on the right. On April 24, 600 cc. of amber cloudy fluid was aspirated from the right side of the chest. On May 1 and 15, a right-sided thoracentesis yielded 850 cc and 200 cc, respectively, of clear, yellow fluid. No tubercle bacilli were demonstrated on smear. Guinea pigs were not available, but on each occasion the fluid was negative for tubercle bacilli on culture. The temperature became normal within 8 weeks, and there was slow improvement. The patient was discharged at her own request on November 3 after 367 days of residence. A chest roentgenogram taken at that time showed thickened pleura or fluid at both bases, extending upward toward the axillas, with mixed infiltration

about the left hilum extending into the 2nd and 3rd interspaces

The patient failed to keep regular clinic appointments, and when seen on August 27, 1945, she had developed severe cough, expectoration, ascites and edema of the ankles. A chest roentgenogram showed exudative infiltration throughout both lung fields, with persistence of marginal pleural reaction consistent with miliary tuberculosis. Sanatorium readmission was advised, but the patient died at home on September 1. Permission for autopsy was not obtained.

*Comment* There was an acute onset of left-sided effusion, with the fluid negative by guinea-pig inoculation, in the presence of suspicious left-sided hilar infiltration, with repeated negative sputum and gastric contents. This was followed by acute right-sided effusion, with a negative culture. The interval between effusions was 6 months. There was eventual development of miliary pulmonary lesions. The cause of death was not ascertained but was undoubtedly tuberculous.

**CASE 7** O P (MCS 796), a 21-year-old, married Negro cook, experienced the gradual onset of a slightly productive cough, dyspnea on exertion, a temperature in April, 1934, of 103°F and weight loss. He was hospitalized elsewhere on May 9, when a chest roentgenogram showed a massive right-sided pleural effusion with cardiac displacement. Thoracentesis on May 11, 1934, yielded yellow-red fluid, with the specific gravity 1.020, the red-cell count 7,000 and the white-cell count 0. By May 28 the fluid had become yellow, with the specific gravity 1.018, the red-cell count 4,000 and the white-cell count 500, all lymphocytes. Intradermal injection of old tuberculin (0.1 mg) was positive. Guinea-pig inoculation of aspirated fluid was negative for tuberculosis. Ten sputum examinations showed no acid-fast organisms.

On August 31, the patient was transferred to this hospital. A chest roentgenogram showed a right-sided pleural effusion, with no evidence of parenchymal disease. A right-sided thoracentesis performed on September 8 yielded 50 cc of clear, greenish fluid, which was negative for tubercle bacilli by guinea-pig inoculation and on culture using Parker's medium. The patient was discharged on November 23 after a total hospital residence of 218 days, 85 of which were spent in this hospital.

He continued well until March 18, 1935, when a small asymptomatic effusion blunting the left base appeared. A thoracentesis performed on April 18, 1935, was unsuccessful. The patient was closely followed in the clinic, and by May 28 the fluid had disappeared. He continued asymptomatic and on October 10, 1944, was essentially well. A chest roentgenogram taken at that time showed a horizontal right diaphragm, but the lungs were clear.

*Comment* There was a gradual onset of right-sided effusion, with the fluid negative by guinea-pig inoculation. This was followed by an asymptomatic transient left-sided effusion. Thoracentesis was unsuccessful. The interval between effusions was 10 months.

## DISCUSSION

The apparent incidence of alternating pleurisy with effusion is low. Among 3822 patients with pulmonary tuberculosis admitted to this sanatorium between September 31, 1931, and September 1, 1945, only 7 cases of alternating pleurisy with effusion were found. During this same interval 48 patients with pleurisy with effusion were admitted. Since Amberson<sup>7</sup> has estimated that in 5 per cent of all cases of pulmonary tuberculosis the serous membranes are involved, it is obvious that only a small percentage of patients with serofibrinous pleurisy are admitted for sanatorium treatment. This is presumably due to the general failure to appreciate both the serious prognosis of serofibrinous pleurisy and the need for sanatorium treatment. Hence, although the statistical incidence of alter-

nating pleurisy with effusion is low, the syndrome is undoubtedly more frequent than is generally realized.

The pathogenesis of alternating pleurisy with effusion is presumably hematogenous. Tuberculous bacilemia is more frequent than is usually appreciated.<sup>8</sup>

## Diagnosis

In the syndrome described, the onset and course of the pleurisy with alternating effusion differed in no way from the onset and course of unilateral serofibrinous pleurisy.<sup>5</sup>

Serofibrinous pleurisy may be of acute or insidious onset, with malaise, fever, cough, variable expectoration and often dyspnea. Ordinarily the active phase of the effusion lasts for four to six weeks, sometimes longer. Occasionally the effusion is transient and asymptomatic, being discovered during routine examination.

The cases presented above show features characteristic of those accepted as clinically diagnostic of so-called serofibrinous pleurisy.<sup>7</sup> As with unilateral pleurisy with effusion, extrapulmonary tuberculosis may precede, accompany or follow alternating pleurisy with effusion.

Thoracentesis is indicated to establish the nature and etiology of a pleural effusion in the absence of obvious systemic disease. The fluid of serofibrinous pleurisy is an exudate. The cells are predominantly lymphocytes, but rarely the fluid is hemorrhagic.<sup>9</sup> Importance, but not pathognomonic significance, can be attached to such a lymphocytosis, for effusions due to carcinoma and to pulmonary emboli may also show this feature.<sup>9</sup>

Guinea-pig inoculation or culture of aspirated fluid is definitely indicated in serofibrinous pleurisy with effusion. Examination of the smear alone for tubercle bacilli is insufficient. In a series of 119 consecutive cases of pleural effusion, occurring chiefly during the course of therapeutic pneumothorax, from different cases routinely studied at the Middlesex County Sanatorium in 1941-1942 and found to be positive for tuberculosis, the fluid in 45 cases was positive—usually Gaffky II or more—on smear (Ziehl-Neelsen stain), and guinea-pig inoculation was accordingly not done. In 7 cases, the fluid was positive on smear and also positive by guinea-pig inoculation. In 67 cases, it was negative on smear but positive by guinea-pig inoculation. Furthermore, of the 24 patients admitted to this sanatorium from 1931 to 1940, inclusive, with a diagnosis of pleurisy with effusion, thoracentesis yielded fluid that was positive (Gaffky II) on smear (Ziehl-Neelsen stain) in only 1 case. In 10 cases the fluid was negative on smear but positive for tuberculosis by guinea-pig inoculation. In 7 cases, it was negative both on smear and by guinea-pig inoculation. In 6 cases, the result of examination was not reported.

Amberson<sup>10</sup> has pointed out that concentration of a larger volume of pleural fluid before guinea-pig

inoculation can logically be expected to increase the percentage of positive tests. On the other hand a negative result of guinea-pig inoculation does not exclude a tuberculous origin. A later aspiration may yield fluid that is positive. In Case 4, the fluid originally aspirated from the left side of the chest was negative for tuberculosis by guinea-pig inoculation but was positive three and a half weeks later. Similarly, in the case reported by Hurrell and Dawson-Walker<sup>2</sup> both fluids originally aspirated were negative but later were positive. Furthermore, as shown in Table 1, there is a high incidence of

TABLE 1 Results of Guinea-Pig Inoculation of Pleural Fluid in Pleurisy with Effusion

AUTHOR	No. of Cases	POSITIVE*	NEGATIVE*
Bonilla <sup>11</sup>	22	7 (2)	15 (7)
Gaard <sup>12</sup>	79	22 (15)	57 (26)
Totals	101	29 (17)	72 (33)
Percentage of cases developing tuberculosis		58	45

\*The figures in parentheses represent patients who later developed tuberculosis, chiefly pulmonary

pulmonary tuberculosis following the development of serofibrinous pleurisy, despite negative results of guinea-pig inoculation.

A final diagnostic procedure that should be used more frequently than at present is guinea-pig inoculation of the fasting gastric content or of sputum if it is being produced. Infrequent cases with a positive guinea-pig inoculation of the gastric content or of sputum in the presence of negative pleural-fluid findings, with no roentgen-ray evidence of pulmonary infiltration, have been observed at this sanatorium.

### Differential Diagnosis

There are numerous causes of pleural effusion. Tinney and Olsen<sup>13</sup> have analyzed 274 cases seen at the Mayo Clinic, with the results indicated in Table 2.

Alternating pleurisy with effusion occurring in the course of such diseases as congestive failure,

A nontuberculous bacterial etiology of the syndrome under discussion has been excluded, since routine cultures of the effusions were negative except, of course, in Case 4, in which was a secondary infection.

Certain relatively infrequent diseases may have to be considered on occasion.

That alternating pleural effusion may be an incident in the course of a polyserositis associated with disseminated lupus erythematosus is admitted. Not one of the cases summarized above, however, showed suggestive skin lesions, leukopenia, albuminuria, pericardial effusion, joint symptoms or other evidence of the characteristic widespread polyserositis associated with disseminated lupus. Furthermore, after variable follow-up periods no suggestive symptoms have developed.

Pulmonary emboli with accompanying effusion may conceivably give rise to the syndrome of alternating pleural effusion. Careful physical examination, with special reference to calf tenderness, presence of Homans's sign and alteration in the diameter of the calf, together with consideration of the associated and characteristic roentgenographic findings,<sup>14</sup> should easily exclude such a possibility.

Severe nutritional disturbances with hypoproteinemia or marked vitamin B deficiency may give rise to serous effusions that are rarely pleural and may possibly simulate the syndrome under discussion.

Chronic constrictive pericarditis — frequently of tuberculous origin — with the characteristic symptoms of dyspnea, abdominal enlargement and often ankle edema may be accompanied by pleural effusion. The fluid is usually a transudate. Similarly, since the fluid of Meigs's<sup>15</sup> syndrome is characteristically a transudate, no diagnostic confusion should arise even though the course of this disease may mimic alternating pleural effusion. Finally, Loeffler's syndrome, characterized by transient, recurrent pulmonary infiltration, a parasitic infestation or an allergic background, a benign clinical course and eosinophilia, has recently been shown to be a rare cause of bilateral pleural effusion and hence a potential cause of alternating pleurisy with effusion.<sup>16</sup> Thus, a twenty-one-year-old man with characteristic infiltration in both lungs developed bilateral pleural effusion. Culture and guinea-pig inoculation were both negative for tubercle bacilli. The fluid from the right side contained 29 per cent eosinophils, and that from the left side contained 64 per cent eosinophils, which appears to be a distinguishing feature.

Exclusion of any of the above conditions should not be difficult if one is familiar with the nature of serofibrinous pleurisy with effusion.

### Treatment

As in acute serofibrinous pleurisy with effusion, the early treatment is symptomatic. Thoracentesis

TABLE 2 Proved Etiology of Pleural Effusion

ETIOLOGY	No. of Cases	PERCENTAGE
Carcinoma	141	51
Congestive failure	42	15
Lymphoma	28	10
Pneumonia	24	9
Tuberculosis	16	6
Cirrhosis of liver	8	3
Chronic nephritis, with nephrosis	7	3
Miscellaneous conditions	8	3
Total	274	

pulmonary infection, polyserositis (Concato's disease), metastatic carcinoma, lymphoma, cirrhosis, septicemia, rheumatic fever or nephritis should be easily distinguished from the syndrome described above and thus offer no difficulty.

is indicated initially for diagnosis and to visualize the underlying lung parenchyma, to relieve respiratory, cardiac or gastric embarrassment produced mechanically and occasionally to help in hastening fluid resorption

Although the acute phase of serofibrinous pleurisy ordinarily lasts for four to six weeks, several months of a sanatorium regime is an essential part of proper treatment Amberson<sup>7</sup> states that serofibrinous pleurisy with effusion should be treated as is active tuberculosis, with sanatorium care Trudeau<sup>17</sup> has shown that the prognosis of pleurisy with effusion with either negative or minimal apical pulmonary findings is excellent in patients receiving at least four months of sanatorium treatment Gaarde's<sup>12</sup> findings are in agreement Obviously, alternating pleurisy with effusion, a variety of acute serofibrinous pleurisy and a manifestation of tuberculosis, should be treated in a comparable fashion, with prolonged bed rest

Chest roentgenograms taken at least semiannually for a period of five years are part of proper follow-up supervision if possible parenchymal infiltration is to be discovered early Since the early infiltration of pulmonary tuberculosis is notoriously silent, both symptomatically and clinically, it is only by frequent roentgenograms that pulmonary tuberculosis following serofibrinous pleurisy can be discovered before extensive progression has taken place.

Prognosis

Alternating pleurisy with effusion may be a disease of serious ultimate significance in the absence of proper treatment Although no conclusions can be drawn from this small group of cases, it appears that a sanatorium regimen or its equivalent is necessary if the likelihood of eventual development of pulmonary or extrapulmonary tuberculosis is to be reduced to a minimum Death from military tuberculosis may be expected in a certain portion of cases of alternating pleurisy with effusion, irrespective of sanatorium treatment.<sup>1, 2</sup>

SUMMARY AND CONCLUSIONS

Seven cases of alternating pleurisy with effusion, defined as the development of serofibrinous pleurisy occurring in the absence of pulmonary infiltration or only with suspicion of it and followed after a variable period of time by the development of contralateral serofibrinous pleurisy, are presented

The onset and course of each effusion associated with this syndrome differ in no way from that of the more frequent unilateral serofibrinous pleurisy

It is shown that alternating pleurisy with effusion may be a manifestation of tuberculosis

The proper treatment of pleurisy with effusion includes a prolonged sanatorium regimen

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## INTESTINAL OBSTRUCTION FOLLOWING ABDOMINAL BATTLE WOUNDS

LIEUTENANT COLONEL PHILIP S FOISIE, MC, AUS\*

IN A previous paper,<sup>†</sup> the management of colostomies secondary to battle wounds of the abdomen has been discussed. Although most of these patients have done remarkably well during their definitive treatment at this general hospital, a few have shown complications that sometimes follow the damage caused by the passage of a ragged shell fragment through the abdomen. These cases should serve as a warning signal to the physicians under whose care such patients may later come.

The necessity of operating on a few of these soldiers has made us conscious of the potential danger of intestinal obstruction. We have been amazed at times that these patients have been able to maintain a functioning intestinal stream in spite of the amount of constriction and angulation of bowel that was found. In such patients particularly, early signs and symptoms suggesting the possible onset of obstruction must receive careful study and evaluation.

Anyone who reads the often penciled and sometimes blood-stained notes of the Field Medical Records is at once struck with the fact that some of these patients lived to reach a general hospital. These records frequently describe intestinal trauma of a severity foreboding almost certain death. The credit for such survivals belongs to the prompt and skillful surgical procedures of the forward medical installations, to the giving of plasma and blood by persons in this country and to the near-miracles of chemotherapy.

Factors that predispose to the formation of adhesions are multiple bowel perforations and lacerations of the bowel, particularly when these have resulted in considerable peritoneal soiling, hemorrhage, blast, lacerations of the mesentery, delay prior to initial surgery and infection. Since battle injuries may involve all these factors, it is not surprising that subsequent obstruction often results.

When some of these patients have been operated on for acute obstruction, an interesting phenomenon in the mechanism of the obstruction has been noted. In civil practice, intestinal obstruction is usually caused by some single discrete difficulty—a strangulated hernia, volvulus, intussusception or the like. The obstruction in these patients, however, is likely to occur partially at several points, with a gradual damming-up effect that increases to the final point of complete obstruction. This building-up of back pressure progresses in the reverse peristaltic direction toward the stomach, until at last so much distention occurs that the bowel becomes twisted or sharply angulated at a point of fixation and total obstruction results. The mechanism of

obstruction is therefore generally that of a series of obstructive points, no one of which is severe enough to cause total obstruction but that together produce a cumulative back pressure, with increasing stagnation of the intestinal stream, until complete obstruction ensues. With the usual obstruction from a single source, correction of the offending mechanism at the point where the bowel changes from distention to collapse solves the problem. In cases with the mechanism described above, on the other hand, the relief of the area of total obstruction frequently only leads one on to another point a few centimeters away distally at which highly questionable function is again encountered.

There is a constant danger in cases of this sort that an enthusiastic surgeon will do too much. The natural desire to free the bowel completely should be curbed, attention being confined to the few points at which some degree of definite obstruction has occurred. Inflamed, fibrin-covered bowel that has been freed is likely to form new adhesions, which may prove a greater hazard than those already freed. A totally obstructed patient should be subjected to as little trauma as will accomplish the goal of the operation—namely, re-establishment of the intestinal stream. Once the obstruction has been relieved, functioning bowel, even though densely adherent, should be left alone. More extensive lysis of adhesions may be attempted later, under more favorable conditions, if symptoms warrant.

Of the many substances that have been used to prevent reformation of adhesions, amniotic fluid has probably been the most successful. It was not available at this hospital, but may be of value in the subsequent treatment of these and similar cases in which further operative procedures are indicated. In several cases, the patients' condition halted mobilization of the bowel before it appeared certain that we had done all that was necessary, but their recovery justified this decision. In other words, a "let well enough alone" policy is applicable to these cases. In some of them we have been surprised on exploration to find with what severe matting together of the entire bowel patients had been able to maintain function until the acute obstructive episode occurred. In some cases, the bowel was so severely involved that complete freeing at a single operative procedure would have been impossible, but once the acute obstructive points were relieved these patients did well. They are, of course, liable to develop similar complications in the future, as are many others who have had intra-abdominal trauma but have so far been able to avoid difficulty. It is safe to predict that in veterans who have suffered abdominal wounds, acute intestinal obstruction will be encountered for many years to come.

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Five case histories will be cited to illustrate the surgical problem involved

**CASE 1** A soldier was wounded in August, 1944, by high-explosive shell fragments, which blew out a large segment of the sacrum, tearing the rectum and causing multiple lacerations of the small bowel. He was operated on at an evacuation hospital through a long midline incision, and several defects in the ileum were repaired. Colostomy was not done at that time. He arrived at this hospital 2 weeks after his injury, at which time most of the feces were being evacuated through the sacral wound. The day after admission a Mikulicz colostomy was performed to divert the fecal stream from the wound. This effort was successful, and with irrigations the wound became clean and was completely healed in 8 weeks, during which time the patient's general condition improved.

The colostomy spur was then crushed and the colostomy was closed. Normal bowel movements followed these procedures, and the patient was apparently ready for evacuation when he developed a sudden and complete obstruction. This event was accompanied by such profound shock that several hours of resuscitative measures were required to prepare the patient for surgery. Under local anesthesia, the colostomy was reopened to ensure complete drainage of the lower bowel. This did not give relief, and after further supportive treatment the abdomen was reopened through a midline incision. Practically the entire bowel was found to be tangled in a mass of adhesions, with only the jejunum and the transverse and descending colon free. With a proximal approach, as much of the small bowel was freed as the patient's condition permitted. This soon proved to be futile, since several portions of the bowel were gangrenous. A catheter was sutured into the most distal point of free, viable small bowel, and the abdomen was closed. The prognosis was obviously hopeless.

At autopsy, performed 2 days later, the entire small bowel from the catheter onward was twisted in a gangrenous mass, which was firmly adherent to the pelvis and flank and also involved the ascending colon. The whole mass had to be resected to disentangle it completely.

*Comment* This case, the only one in the present series that terminated fatally, demonstrated the extreme involvement of bowel that may occur.

**CASE 2** The patient, a 20-year-old soldier, was wounded on November 12, 1944, by mortar-shell fragments, which caused multiple injuries, including penetration of the abdomen and multiple wounds of the small bowel. There was considerable inter-abdominal bleeding. At operation on November 22 at an evacuation hospital, the lacerated bowel was sutured. Colostomy was not done. Infection of the abdominal wound ensued.

On admission to this hospital on December 9, the patient was running a septic type of temperature and complained of pain in the right inguinal region. Chemotherapy and supportive treatment were used, pending a clearer indication for surgery, until December 13, when acute localized tenderness developed in the right lower quadrant of the abdomen, with definite muscle spasm. Laparotomy was performed on this date through the old wound, which was paper thin and was not completely healed. A diffuse fibrinous peritonitis was found, with free pus throughout the abdomen, multiple small walled-off abscesses and severe matting of the bowel by extensive adhesions. The abscess cavities were broken up, and drains were inserted through a stab wound into the pelvis. Although obstruction seemed unavoidable, the patient never developed any signs of it and became afebrile within 10 days. He was evacuated to the Zone of Interior on January 6, 1945, in good general condition.

*Comment* This case, in which there was no actual obstruction, illustrates well the peritoneal difficulties that may follow abdominal battle wounds. There was every reason to expect obstruction, which demonstrates what extensive disease may be tolerated, with maintenance of intestinal flow, provided that the adhesions are innocuous. This patient is of course liable to have subsequent complications.

**CASE 3** A 23-year-old soldier was wounded in Germany on December 7, 1944, by high-explosive shell fragments, which caused multiple wounds, including an abdomino-thoracic injury with severe right hemothorax, perforation of the right diaphragm and liver and considerable intra-

abdominal bleeding, but no bowel perforation. He was operated on at a field hospital on the day of the injury. The abdominal wound was closed after the evacuation of considerable blood, and drainage to the right subphrenic area was established through a stab wound in the flank. Thoracotomy was done, with repair of the rent in the right diaphragm.

The patient was admitted to this hospital on December 25 and appeared to be convalescing satisfactorily. On December 29, he developed sudden severe pain in the left lower quadrant of the abdomen and shortly presented signs of total intestinal obstruction. Laparotomy revealed multiple adhesions, which tied the bowel at several places, from the ilio-cecal valve through the distal third of the ileum to a point at which a loop of small bowel was anchored and twisted into a volvulus in the left lower quadrant. A loop of terminal ileum was firmly adherent at a point deep in the pelvis, and the freeing of this loop completely relieved the obstruction. The patient made an excellent recovery, in spite of being given doughnuts and coffee by a fellow patient on the 3rd postoperative day.

*Comment* This case demonstrates the development of a total obstruction secondary to abdominal injury with no bowel perforation. The adhesions apparently developed from a retained blood clot.

**CASE 4** The patient, a Negro soldier, sustained abdominal wounds, which had been treated at another general hospital for several weeks. On the way to the Zone of Interior, while lodged for the night at this hospital, he developed abdominal pain, distention, vomiting and acute localized tenderness and spasm. Obstruction was considered certain. Laparotomy disclosed the multiple-gradient type of obstruction described above, with the final point of total obstruction at a point in the left flank, to which a loop of twisted small bowel was securely fixed by a dense adhesion. Section of these adhesions gave complete relief.

**CASE 5** A 28-year-old soldier was wounded on April 18, 1945, by a rifle bullet, which entered the right buttock and transversed the abdomen, making its exit through the left lower quadrant of the anterior wall. In its course the lower end of the right ureter was severed 3 cm above the vesical orifice. Two loops of small bowel were sufficiently injured to require resection and end-to-end anastomosis. There were also a compound fracture of the right ilium and extensive retroperitoneal hemorrhage.

The initial bowel repair was done at an evacuation hospital on the day of injury. The patient was subsequently treated at another general hospital, and was about to be evacuated to the Zone of Interior when the station hospital was ordered closed and he was transferred here to this hospital.

At admission on May 22, the patient presented a soft abdomen, with a nearly healed abdominal scar showing some evidence of recent infection. There was a urinary fistula through the right buttock.

One week after admission, colicky abdominal pain, with nausea, vomiting and increasing distention suddenly developed. Wangenstein suction gave no relief, and since the symptoms were rapidly progressing, operation was performed 3 hours after the onset of the acute attack. The old midline scar was excised, and when the abdomen was opened a generalized fibrinous peritonitis was found. This was most acute in the right lower quadrant, where multiple loops of bowel were matted together, apparently in an attempt to wall off urinary leakage from the severed ureter. The bowel, including the large bowel as far down as the sigmoid, was distended.

The adherent loops in the right lower quadrant were freed, a catheter was sutured into the cecum and brought out through a stab wound, and the wound was closed with heavy silk sutures without drainage. Ochsner treatment was instituted, with 40,000 units of penicillin in each infusion.

On the 10th postoperative day, the patient was doing well. The abdomen was soft, with no distention. Flatus was being expelled by rectum, and the temperature, pulse and respirations were normal. It was planned, as soon as the patient's condition permitted, to drain the kidney pelvis so as to remove the source of the peritonitis.

*Comment* Although much of the distention was due to peritonitis, it seems probable that this patient had an acute obstruction due to the fact that the distended bowel was

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fluid protein. Accordingly, the patient was thought to have an associated diabetic neuritis. His course had been essentially uneventful, however, and he was discharged on a dosage of 40 units of protamine-zinc insulin and a diet consisting of 129 gm. of carbohydrate, 69 gm. of protein and 76 gm. of fat.

The patient was regularly followed in the Diabetes Clinic for the next 3 years. He then disappeared for 3 years, reappearing in the Emergency Ward in April, 1943, with severe diabetic acidosis, precipitated by a throat infection. The blood sugar was 434 mg. per 100 cc., the carbon dioxide content 18.5 millimols per liter, and the blood nonprotein nitrogen 64 mg. per 100 cc. He was given 388 units of crystalline insulin (124 units intravenously), 4500 cc. of 5 per cent dextrose in normal saline solution and 15 gm. of sodium bicarbonate. The acidosis responded well, but the patient ran a stormy course and developed severe respiratory distress, which necessitated an emergency tracheotomy on April 28, 1943. He was later found by x-ray to have complete laryngeal obstruction. Throat cultures showed a hemolytic *Staphylococcus aureus* to be predominating, and he was therefore given sulfadiazine for 2 weeks. Since the tracheotomy incision could not be closed because of the laryngeal obstruction, he was discharged on June 22 with the tube in place. The insulin requirement at that time was 30 units of protamine-zinc insulin and 10 units of crystalline insulin every morning, with occasional extra crystalline insulin by test.

In the following November, the patient was readmitted for widening of the tracheotomy. Three operations were later performed in an unsuccessful attempt to close the tracheotomy permanently. At that time it was extremely difficult to regulate the diabetes. The patient was discharged on a dosage of 40 units of globin insulin and a diet of 225 gm. of carbohydrates, 85 gm. of protein and 90 gm. of fat.

Throughout the next year, he appeared at irregular intervals in the Diabetes Clinic and was seen there on August 4, at which time the urine showed an orange color on a Benedict test.

The patient's living conditions had been extremely poor. He lived alone and prepared his own meals, living chiefly on canned foods and paying little attention to the prescribed diet. He was unwilling to work at his former trade of weaving because the tracheotomy made him self-conscious, and his sole interest in life was to return to the hospital to have it repaired. As months went by without word of an appointment, he became more and more depressed and lost the desire to live. He denied alcoholic indulgence during this time, but admitted almost complete neglect of his diabetes treatment.

The fifth admission occurred on January 3, 1945, when the patient was brought to the Emergency Ward by ambulance in a semicomatose condition. Two days previously he had developed abdominal pain, nausea, vomiting and diarrhea. He had been taking insulin — 80 units of globin insulin — "fairly regularly" but had not tested his urine for some weeks. The diet had consisted largely of canned foods in irregular amounts. The night before admission he called a physician, who suspected an impending diabetic coma but gave no extra insulin. On the morning of admission, in addition to the symptoms listed, the patient had suddenly become deaf and was unable to hear unless one shouted directly into either ear.

The physical examination revealed a thin, pale and semicomatose patient. The skin and tongue were dry. The eyeballs were soft. The breath smelled of acetone. The patient could be aroused only with difficulty and spoke in a hoarse voice when he closed the tracheotomy tube. There were a few coarse rales at both lung bases, but no abnormal breath sounds. The heart was not enlarged. The rhythm was totally irregular, and the heart sounds were of poor quality. No murmurs were heard. The abdomen was soft, but there was generalized tenderness without rebound or spasm. The liver, spleen and kidneys were not felt. Deep-tendon reflexes were absent on admission.

The temperature was 95.8°F., the pulse 140, the respirations 40 (Kussmaul), and the blood pressure 80/50.

The urine gave a brick-red test for sugar and ++++ tests for acetone and diacetic acid and contained a slight trace of albumin. Its specific gravity was 1.022. The hemoglobin was 12.7 gm. per 100 cc., the red-cell count 4,300,000, and the white-cell count 22,700. The blood-sugar level was 1240 mg. per 100 cc. and the carbon dioxide was 3.8 millimols per liter. The nonprotein nitrogen was 108 mg. per 100 cc.,

the chlorides 76 milliequiv. per liter, and the total protein 8.2 gm. per 100 cc.

Therapy was started immediately with 1500 cc. of normal saline solution intravenously, 100 units of crystalline insulin — 50 units intravenously and 50 subcutaneously — and 15 gm. of sodium bicarbonate. The stomach was aspirated, but no fluid was obtained. This was a rather hazardous procedure, and the patient struggled against it so much that he became cyanotic owing to improper functioning of the tracheotomy tube. An indwelling catheter was inserted shortly after admission, and 1000 cc. of urine was obtained. A second infusion was started with 250 cc. of blood plasma in saline. When the blood chemical findings became available 1½ hours after admission the insulin dosage was increased to 100 or 200 units intravenously and 100 or 200 units subcutaneously hourly, thus during the first 3 hours the patient received a total of 720 units. Despite the giving of constant intravenous saline solution with alkali, he remained anuric for 6 hours. Accordingly, blood chemical analyses were checked at hourly intervals. After an initial fall from 1240 mg. per 100 cc. to 928 mg., the blood-sugar level remained at approximately 900 mg. for 4 hours, necessitating constantly increasing doses of insulin. At 2:30 p.m., 4 hours after admission, the patient became extremely cyanotic and dyspneic. The pulse could not be obtained, and the respirations ceased. Oxygen and artificial respiration were given, and 3 cc. of a 25 per cent solution of Coramine and 0.5 gm. of caffeine sodium benzoate were injected intravenously, after which the respirations and pulse returned. The insulin dosage was increased to 200 units every half hour — 100 units intravenously and 100 subcutaneously — in a desperate attempt to lower the blood sugar and correct the ketosis. At 4:30 p.m. an increase in the number of rales in the lungs was noted, and in view of the auricular fibrillation, which was confirmed by electrocardiogram, digitalization was begun at once with 6 cc. (12 mg.) of Cedilanid intravenously. Shortly after this, 5 cc. of urine was obtained. In an attempt to produce a diuresis, 20 cc. of a 10 per cent solution of serum was given at 5:10 p.m. Thereafter the patient's condition steadily improved, the insulin dosage was lowered, and at 4 a.m., 18 hours after admission, the blood sugar was 119 mg. per 100 cc., the carbon dioxide 37.1 millimols per liter, the nonprotein nitrogen 72 mg. per 100 cc., and the chloride 95 milliequiv. per liter. The last dose of insulin (50 units) was given at 3 a.m. At 6:30 a.m. there was a mild insulin reaction, with the blood sugar 35 mg. per 100 cc., which was relieved by 50 cc. of 50 per cent glucose intravenously. The summary of therapy during the first 20 hours is given in Table 1. The

TABLE 1 Summary of Therapy Given During the First Twenty Hours

SUBSTANCE	QUANTITY
Crystalline insulin	3620 units ( $\frac{1}{2}$ intravenously, $\frac{1}{2}$ subcutaneously)
Normal saline solution	7000 cc. (intravenously)
Sodium bicarbonate	52.5 gm. (intravenously)
Blood plasma	1500 cc. (intravenously)
Whole blood	250 cc. (intravenously)
Cedilanid (Lanatonide C)	1.6 mg. (intravenously)
Coramine	0.75 gm. (intravenously)
Caffeine sodium benzoate	0.5 gm. (intravenously)
10% saline solution	20 cc. (intravenously)
Broth and fruit juice	800 cc. (orally)

total fluid intake during the first 20 hours was 9630 cc., and the output was 2035 cc., exclusive of the 1000 cc. obtained when the patient was catheterized shortly after entry.

On the following day, the patient continued to complain of abdominal pain and was unable to eat. He was fed by intravenous fluids and required only 40 units of insulin throughout the day. The hearing had returned to normal. The heart rhythm had also returned to normal, — this was confirmed by electrocardiogram, — and it was thought that digitalis was no longer necessary. Blood-sugar samples taken throughout the day varied between 52 and 171 mg. per 100 cc., and the carbon dioxide had begun to return to normal (Table 2).

The abdominal pain persisted for 4 days, but on January 7 the patient was able to eat and an attempt to regulate the diabetes was begun. This proved to be quite difficult, and various combinations of protamine-zinc, crystalline and

caught in adhesions in the right lower quadrant, secondary to urinary leakage

### SUMMARY

Abdominal battle injuries are likely to produce extensive adhesions that pave the way for subsequent obstruction. Such patients may do well for varying periods, but a serious hazard persists, and obstructive episodes will probably be encountered for years to come.

Early signs and symptoms should receive careful evaluation and close watching.

A graduated obstructive mechanism is described. With acute obstruction only the offending mechanism should be freed. Interval lysis with the instillation of amniotic fluid may be advisable when chronic symptoms suggest impending difficulty. Five illustrative cases of acute intestinal obstruction, with 1 death, are reported.

## SUCCESSFUL TREATMENT OF SEVERE DIABETIC COMA COMPLICATED BY CHRONIC LARYNGEAL OBSTRUCTION\*

### Report of a Case

ROSEMARY V. GORMAN, M.D.,† REED HARWOOD, M.D.,‡ AND PAUL D. WHITE, M.D.§

BOSTON

THE association of severe diabetic coma and chronic laryngeal obstruction is rare. The case reported herein presented these two problems, and in addition a third, a severe mental depression following tracheotomy that induced the patient to neglect the treatment of his diabetes. Although his immediate survival depended on recovery from the coma, his return to life as a useful citizen awaited the repair of the tracheotomy. In the treatment of the coma, the largest amount of insulin ever reported to have been given in twenty hours was administered. Three delicate plastic operations were performed to repair the tracheotomy. Our experience with such a patient is worth recounting, in the hope that it may be a means of rescuing others from death or despondency.

There are many reports in the medical literature of extreme hyperglycemia requiring tremendous doses of insulin. These cases can be divided into two groups. In the first, hyperglycemia is usually associated with coma and its cause is evident — infection, hepatic disease, endocrine disorder or neglect of insulin therapy or diet. The acidosis is controlled by large doses of insulin, and the patient usually returns to his precoma status. In the second group, in which also the condition may be associated with coma, there is no explanation for the obstinate hyperglycemia, and the need for excessive doses of insulin continues for weeks or even months. This group is composed of patients who may be called insulin-resistant. It will not be further discussed here.

The case reported presents several unusual features. The coma was precipitated by infection and neglect of insulin therapy. The infection was apparently a severe, nonspecific gastroenteritis. The

patient received 3620 units of insulin in twenty hours. In Wiener's<sup>1</sup> case the patient required 3250 units of insulin in the emergency, but the case differed from the present one in his continued need for large doses of insulin. In a case reported by Glass, Spingarn and Pollack,<sup>2</sup> the patient required 85,000 units over a five-and-a-half-month period and the maximum twenty-four-hour dose was 2795 units. It is interesting that the excessive insulin need subsided six months after its onset. The greatest daily quantity of insulin given at the New England Deaconess Hospital has been 2272 units in the case of a man who had diabetic coma during a phase of insulin resistance.<sup>3</sup> Many cases, however, have been reported in which the initial blood-sugar levels exceeded that of 1240 mg per 100 cc in the present case. The highest value recorded is 2060 mg.<sup>4</sup> Dillon and Dyer<sup>5</sup> reported the highest blood-sugar level (1850 mg) recorded in a patient who survived.

### CASE REPORT

C. D., a 34-year-old man, a native of Massachusetts, was admitted to the Massachusetts General Hospital for the fifth time on January 3, 1945, semicomatose and in severe diabetic acidosis.

The patient was first admitted to this hospital on April 10, 1929, for regulation of his diabetes, which had been discovered in 1924, when he was 14 years old. In 1925, his physician had started him on insulin, gradually increasing the dose and varying the diet to suit the patient's needs. He did not co-operate well and was therefore hospitalized. After 10 days of study, he was discharged on a diet consisting of 120 gm of carbohydrate, 180 gm of protein and 100 gm of fat and a dosage of 50 units of insulin (20-20-10).

He did well thereafter until 1935, when he was readmitted to the Orthopedic Service with a fracture of the right tibia and fibula and phenobarbital poisoning. At this time the diabetes was slightly more difficult to control, and the patient was discharged on a dosage of 51 units of crystalline insulin (25-5-15-6) and a diet consisting of 160 gm of carbohydrate, 92 gm of protein and 101 gm of fat.

The third admission occurred in 1936, and was for tonsillectomy and diabetic regulation on protamine-zinc insulin. There had been some abnormal neurologic findings, — sluggish knee and ankle jerks and equivocal plantar responses, — and lumbar puncture revealed an elevated spinal

\*From the Medical Service of the Massachusetts General Hospital.

†Assistant in medicine, Massachusetts General Hospital.

‡Assistant physician, Massachusetts General Hospital.

§Physician, Massachusetts General Hospital.

these probably contributed to the patient's recovery from a moribund state, as did also the artificial respiration

The reconstruction of the air passages,—the trachea and larynx,—an extremely delicate but successful therapeutic procedure was of great importance in the maintenance of morale and of the

of insulin in twenty hours Other unusual features were deafness and auricular fibrillation, both of which quickly cleared up

Because the patient was prone to neglect his daily treatment as a result of a mental depression caused or aggravated by a long persisting tracheotomy, a series of three delicate plastic operations to

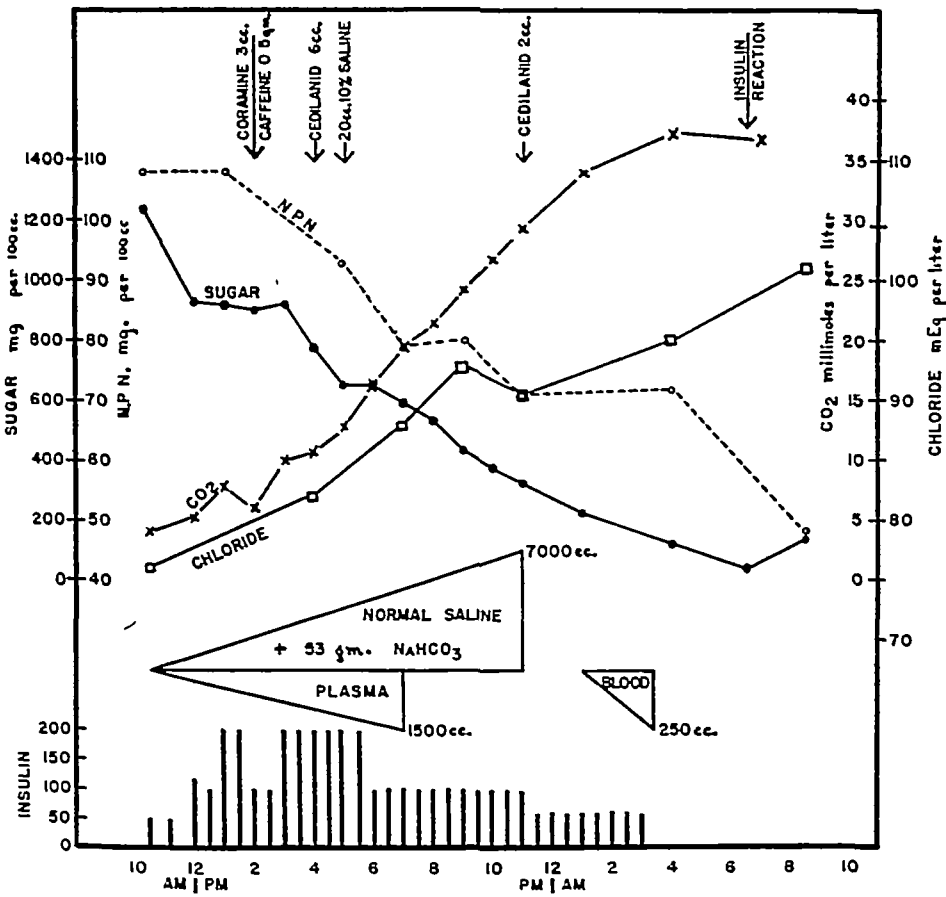


FIGURE 1

desire for life after recovery At first it was suggested that the patient's condition presented too great a risk or at least promised too short a survival time to warrant the hazard, but the reverse seemed likelier to be true — namely, that the repair of the air passages would make life again worth living, and hence that so far as the diabetes, and with it the patient's longevity, was concerned, the risk of not operating would actually be greater than the risk of operating This prophecy has so far proved to be correct

SUMMARY

The case is reported of a man of thirty-four in diabetic coma who required for recovery 3620 units

repair the air passages were carried out to rehabilitate him after recovery from diabetic coma This has undoubtedly been as important in aiding the patient's longevity as was the immediate treatment of the diabetic coma

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globin insulin were tried. The disease was finally under fairly good control with 35 units of protamine-zinc insulin every morning. On this dosage the urine varied between green, with sediment, and blue, the fasting blood sugar was 105 mg per 100 cc on one occasion and 152 mg on another.

On February 16, 45 days after admission, the patient was transferred to the Massachusetts Eye and Ear Infirmary for a plastic operation on the trachea, in an attempt to close the tracheotomy and thus remove the factor responsible for the mental depression. Two operations were performed in the preparation of skin flaps on the right and left sides of the neck. In the right-hand flap several strips of cartilage were embedded to give added support to the trachea. The tube was left in place, and on April 7 the patient was discharged.

hospital. Deafness was an unusual complication of the coma and could not be explained. No reference to this concomitant appears in the literature. Another unusual feature was the occurrence of auricular fibrillation, which so far as we know has been reported in only 1 other case of diabetic coma.<sup>3</sup> In both cases the fibrillation was transient and recovery from the coma was complete.

It has been suggested, on review of the data, that this patient was overtreated. This is admitted, but

TABLE 2 *Insulin Dosage and Blood Chemical Findings*

DATE	TIME	DOSE OF INSULIN	BLOOD CHEMICAL FINDINGS				
			SUGAR	CARBON DIOXIDE	NONPROTEIN NITROGEN	CHLORIDE	TOTAL PROTEIN
		units	mg /100 cc	mM /l	mg /100 cc.	mE /l	gm /100 cc
1/3/45	10 30 a m	50	1240	3.8	108	76	8.2
	11-00	50					
	12-00 noon	120	928	5.2			
	12 30 p m	100					
	1-00	200	920	7.9	108		
	1:30	200					
	2-00	100	900	6.0			
	2 30	100					
	3-00	200	920	9.9			
	3 30	200					
	4 00	200	776	10.6		82	6.2
	4 30	200					
	5 00	200	652	12.8	93		
	5 30	200					
	6-00	100	652	16.3			
	6 30	100					
	7 00	100	592	19.3	79	88	
	7 30	100					
	8-00	100	532	21.4			
	8 30	100					
	9 00	100	436	24.2	80	93	
	9 30	100					
	10-00	100	376	26.7			
	10 30	100					
	11-00	100	326	29.3	71	91	6.2
	11 30	50					
1/4/45	12-00 midnight	50					
	12 30 a m	50					
	1-00	50	220	33.9			
	1 30	50					
	2 00	50					
	2 30	50					
	3 00	50					
	4-00		119	37.1	72	95	
	6 30		35	36.7			
	8 30		131	38.2	47	101	5.5
	12 45 p m.		103	36.7	46	100	
	4 30		52	37	40		
1/5/45	9 00 a m.		171	34.3			
	9-00 a m.		109	34.8	37	102	5.5
1/6/45	3-00 p m.		200	30.9			
	9 00 a m.		33	32.4	30	92	5.7
	5-00 p m.		260	24.5			

home on a dosage of 30 units of protamine-zinc insulin and 15 units of globin insulin every morning and a diet of 300 gm of carbohydrates, 100 gm of protein and 80 gm of fat.

On June 2, the patient was readmitted to the Eye and Ear Infirmary, where the tracheotomy was successfully closed at a third operation by incising around the edges of the opening and suturing them over it, and swinging the previously prepared delayed flap from the right side of the neck over the tracheotomy.\* No change was made in the satisfactory program used for the regulation of the diabetes, and on June 20 the patient was discharged asymptomatic and in good spirits.

### DISCUSSION

This patient had a severer diabetic acidosis and required more insulin in the first twenty-four hours than has any other patient ever treated in this

with qualification. The insulin dosage was large but not excessive. If larger doses had been given early the total dose required might have been smaller. Doubtless larger doses should have been administered at once, even before the blood analysis was reported. The dosage of sodium bicarbonate was perhaps excessive, but it caused no irreversible changes. The fluid intake, in view of his severe dehydration and nausea, was not excessive. The question of whether the blood and plasma were necessary is one of pure speculation. The patient's condition was such that they could not well have been omitted. Likewise, the oxygen, Coramine, caffeine, Cedilanid and hypertonic saline solution were given under definite indications. Each of

\*These operations will be described in detail in a later publication by Dr V. H. Kazanjian to whom we are indebted for this account.

the point of an experimental coarctation of the aorta. Since the operation to be described was devised to compensate for an inadequate flow of blood to the lungs, it seemed desirable that the anastomosis be made in such a manner that the blood from the systemic artery would be enabled to reach both lungs. Suture anastomosis could not be made to the main pulmonary artery, since occlusion of this vessel for more than a few minutes causes death. It therefore appeared that the anastomosis should be made just distal to the division of the main pulmonary artery and, furthermore, that the side of the chosen vessel should be used so that the blood might flow to both lungs.

With such an extensive clinical and experimental background, briefly summarized above, Blalock operated successfully on 3 patients, all of them children, who had a clinical diagnosis of tetralogy of Fallot with a severe degree of pulmonary stenosis. There were slight variations in each of the operations, but the following abbreviated description summarizes the major features.

Under light general anesthesia, an anterior transpleural approach was made on the right or left side, depending on the position of the great vessels and the artery to be used in the anastomosis. The right or left pulmonary artery was exposed and dissected from the adjacent tissues for as great a distance as possible. The subclavian or innominate artery was dissected free of the adjacent tissues, and by the use of a bulldog arterial clamp the vessel chosen was occluded temporarily at the point at which it arose from the aorta. In the case of the innominate artery, its branches were ligated at their origins and it was cut across just proximal to the ligatures. A bulldog arterial clamp was placed on the right or left pulmonary artery just distal to the point of division of the main pulmonary artery. A second clamp was placed on the right or left pulmonary artery just proximal to the point where the vessel gave off a branch to the upper lobe of the lung. A transverse opening was made into the side of the pulmonary artery midway between the two clamps. The anastomosis between the end of the systemic artery and the side of the pulmonary artery was then carried out, with a meticulous technic and with the employment of fine silk on a curved needle as suture material. The bulldog clamps were removed from the pulmonary artery, and this was followed by removal of the clamp from the systemic vessel. The lung was re-expanded, and the incision in the chest wall was closed.

Each of the 3 patients suffered from such a severe degree of pulmonary stenosis that there was inadequate circulation to the lungs. Although the three operations differed in detail, in each case the procedure greatly increased the volume of blood that reached the lungs.

Fear that an intensely cyanotic patient would not tolerate a long operative procedure in which

it was necessary to open the pleural cavity and to occlude temporarily one of the pulmonary arteries proved unfounded. Fortunately, the administration of oxygen during anesthesia increased the oxygen content of the arterial blood, and cyanosis was definitely lessened. The question whether a patient already severely anoxic would tolerate the occlusion of one of the main pulmonary arteries for the period necessary in performing the anastomosis appears to have been answered satisfactorily. The 3 patients tolerated occlusion of the left or right main pulmonary artery for periods of thirty to ninety minutes.

Another question that arose was whether ligation and division of the left subclavian artery or the innominate artery would result in serious impairment of the circulation to the arm and brain. Blalock and Taussig were gratified to note that there was little evidence of impairment of circulation to the parts deprived of their major arterial pathway. The pulse was absent for some time postoperatively, and the part was slightly cooler than the corresponding one on the opposite side of the body, but immediately after operation it was evident that the circulation was adequate to maintain life in the part. The advisability of performing upper dorsal sympathectomy at the time of operation, which does not add to the burden of operation, is suggested by the authors.

Blalock and Taussig state that the degree of impairment in the flow of blood to the lungs varies from patient to patient and that the selection of the vessel to be used depends on the extent of the need of the patient for an increase in the circulation to the lungs. The size of the vessel chosen and of the anastomosis itself should not be larger than is necessary for the relief of anoxemia, because of the danger associated with excessive shunting of blood to the lungs.

A discussion of other methods by which an anastomosis between the systemic and pulmonary circulations may be made includes a simple and rapid method that Blalock and his associates<sup>3, 4</sup> have carried out in experimental animals. The first portions of the medial walls of the aorta and the pulmonary artery, which are intimately adherent to each other, are contained within the pericardial cavity and are enclosed in a tube of serous pericardium common to the two vessels. They were able to produce a fistula between the two vessels in dogs by inflicting a stab wound in this region. The knife blade was introduced through the opposite free wall of the pulmonary artery, the walls of the pulmonary artery and aorta, which were in intimate contact, were pierced, the knife was withdrawn, and the opening in the free side of the pulmonary artery was closed by sutures. The establishment of the fistula required only a few seconds. The method is mentioned because it may be necessary to use the major blood vessels and to employ considerable speed if

## MEDICAL PROGRESS

### SURGERY OF THE HEART AND STRUCTURES RELATED TO IT

JOHN W. STRIEDER, M.D.\*

BOSTON

**S**URGERY of the heart and structures related to it will be considered under five main headings — congenital lesions, trauma, acute pericarditis, constrictive pericarditis and miscellaneous conditions

#### CONGENITAL LESIONS

##### *Pulmonary Stenosis or Pulmonary Atresia*

Blalock and Taussig<sup>1</sup> have recently reported and discussed 3 cases in which children with severe degrees of pulmonary stenosis were operated on successfully and with apparent benefit. Heretofore, there has been no satisfactory treatment for pulmonary stenosis or pulmonary atresia. A so-called "blue baby" with a malformed heart was considered beyond the reach of surgical aid. These authors in undertaking the operation were convinced that even though the structure of the heart was grossly abnormal, it might be possible in many cases to alter the course of the circulation in such a manner as to lessen the cyanosis and the resultant disability. They emphasize the fact that it is not the cyanosis per se that does harm.

In the development of this thesis, the studies of Lundsgaard and Van Slyke<sup>2</sup> on the causes of cyanosis are cited. These studies demonstrated the great significance of pulmonary factors. The extent of the oxygenation of the blood in the lungs clearly depends on the vital capacity of the patient, the rate of flow of blood through the lungs, the partial pressure of the oxygen in the inspired air and a specific pulmonary factor that is designated as the "alpha factor." In most, if not all, cases in which there was a pronounced polycythemia, there were secondary changes in the lungs of such a nature that all the blood that passed through them was no longer in effective contact with the oxygen in the alveoli. The fact that all the blood that circulated through the lungs was not fully oxygenated made it seem improbable that if more blood had circulated through the lungs a larger proportion of it would have been oxygenated. Blalock and Taussig believe that this demonstration of the alpha factor completely overshadows another vitally important factor — namely, the volume of blood that reaches the lungs for aeration.

Expressed in the simplest terms, the circulation of the blood through the lungs after birth is essential for life, anyone deprived of such circulation dies. For example, in all cases of pulmonary atresia in which the circulation to the lungs is by way of the

ductus arteriosus, the closure of the latter renders the condition incompatible with life.

Blalock and Taussig then discuss a variety of congenital malformations that illustrate the importance of the volume of the pulmonary circulation in the production of cyanosis. One of these is the malformation consisting of a single ventricle with a rudimentary outlet chamber. If the great vessels occupy their normal positions, the aorta arises from the common ventricle and is of large caliber, whereas the pulmonary artery arises from the rudimentary outlet chamber and is of small caliber. As a result, a large volume of blood goes to the systemic circulation and only a small volume of blood goes to the lung, and there is intense cyanosis. If the great vessels are transposed and the pulmonary artery is large and the aorta is small, a large volume of blood goes to the lungs for aeration, and cyanosis is minimal or absent.

Another case in point is that of truncus arteriosus. When the pulmonary arteries arise directly from the aorta, there is adequate circulation to the lungs, and cyanosis is minimal or absent. If, however, the pulmonary artery fails to arise from the heart or to connect with the aorta and the circulation to the lungs is by way of the bronchial arteries, only a small volume of blood reaches the lungs for aeration, and cyanosis is intense.

As a result of these and other observations, these authors conclude that many gross malformations of the heart are compatible with life provided there is adequate circulation to the lungs and, furthermore, that lack of circulation to the lungs is the primary cause of death in many infants with congenital malformation of the heart. An appreciation of these facts, together with an extensive previous experience with the experimental use of large arteries for the purpose of conducting blood to sites not usually supplied by such vessels, led to the development of an operation for increasing the flow of blood through the lungs in patients with congenital malformations of the heart. The operation consists in making an anastomosis between a branch of the aorta and one of the pulmonary arteries, — in other words, the creation of an artificial ductus arteriosus.

Levy and Blalock<sup>3</sup> have demonstrated the feasibility of anastomosing a systemic artery to one of the pulmonary arteries in experimental animals. Blalock and Park<sup>4</sup> have reported the suturing of the severed proximal end of the subclavian artery to the aorta as a means of conducting blood beyond

\*Visiting surgeon in charge of thoracic surgery, Massachusetts Memorial Hospitals and Boston City Hospital; assistant professor of thoracic surgery, Boston University School of Medicine.

was undertaken. The aorta was ligated with 1 3 cm-wide cotton tape just below the left subclavian artery and 4 cm below the aneurysm. The divided ends of the aorta were oversewed with silk.

The convalescence was uneventful until the seventeenth day, when acute cardiac decompensation occurred. This was treated satisfactorily with oxygen, morphine, venesection, digitalization, mercuripurin and ammonium chloride. The patient was discharged on the thirty-sixth postoperative day.

The pathogenesis of the aneurysm was not definitely established, but the authors consider it necessary to assume the presence of a coarctation to explain the remarkably well developed collateral circulation, the bilateral rib notching and the absence of pulsation of the aneurysm and of the aorta below it.

The success of this operation was attendant on a happy combination of circumstances, and it is extremely unlikely that this combination will again be encountered. As the authors point out, this case was unique in that all the factors essential to the success of the operation were present — youth and general good health, the absence of syphilitic disease of the aorta, the presence of a well established collateral circulation and the favorable location of the aneurysm, which permitted the placing of the proximal ligature on the aorta below the left subclavian artery.

The authors also emphasize that the success in their case has no bearing on the management of aneurysm in general.

#### *Patent Ductus Arteriosus*

The literature on patent ductus arteriosus continues to increase, and as might be expected with the availability of larger series of cases that have been treated by ligation, certain authors have attempted to determine the need for surgery in these cases. Shapiro and Keys<sup>8</sup> discuss a clinical series of 51 cases and analyze operations undertaken for ligation of the patent ductus in 140 cases. During their years of observation, they have been led to consider the lesion an apparently harmless one. Children have gone through school, young men have done hard labor and women have borne children, all with no evidence of cardiac disability. On the basis of these observations, one may readily assume an attitude of conservatism. Analysis of the world literature, however, showed that 80 per cent of patients eventually die from their cardiac lesion. Those who were alive at seventeen years of age averaged thirty-five years at death. At least 40 per cent of these patients died of subacute bacterial endarteritis, and most of the remainder died of congestive heart failure. The average age of the authors' series of 51 patients was less than twenty-five years, and the oldest patient died at fifty-eight. These data force reconsideration of a conservative attitude toward what might seem radical surgery.

The authors conclude that surgery is advisable for most patients with patent ductus arteriosus, with or without subacute bacterial endarteritis. Ligation should be attempted immediately once a diagnosis of subacute bacterial endarteritis has been made.

Burch<sup>9</sup> states that ligation should be done if there is associated endarteritis, and also if there is progressive cardiac damage and decompensation or definite impairment of mental and physical development. He reviewed most of the reported cases of surgical ligation and found the mean mortality rate to be 8.5 per cent in uninfected cases. Burch believes that in the future the operation will probably be recommended as soon as a patent ductus is discovered, but in view of the mortality no such recommendation can be made now. Poor results following ligation, he states, may be attributed to failure to find the ductus, ligation of the wrong vessel, wound sepsis, hemorrhage, associated cardiovascular abnormalities and incomplete obliteration of the ductus.

Such a reactionary attitude does not seem fully justified. The operation is still technically in its developmental stage, and most thoracic surgeons are of the opinion that a considerable reduction in the operative mortality is by no means beyond achievement. Of course, only time will tell how ligation will affect the life span.

The effect of ligation on infection of a patent ductus has been dramatic, and infection must now be considered an urgent indication for operation. Tubbs<sup>10</sup> describes 9 cases of subacute bacterial endarteritis complicating this anomaly and treated by ligation. Six of the patients were well fifteen months to four years after operation. He stresses the importance of the early diagnosis of the super-vention of infection so that ligation may be undertaken at the optimum time, before the infection has had an opportunity to render the ductus friable and the adjacent tissues edematous.

Bettman and Tannenbaum<sup>11</sup> report the successful ligation of a patent ductus complicated by bacterial endocarditis in a woman eighteen years old. She made a good recovery and was well two years after operation. Harper and Robinson<sup>12</sup> treated a similar case in a woman of twenty-eight who had long-standing severe subacute bacterial endocarditis. The ductus was ligated with two silk ligatures, and cellophane was wrapped loosely about it. These authors believe that the cellophane was responsible for the final complete occlusion of the ductus. The murmur and symptoms disappeared for two weeks, but reappeared and persisted for two and a half months after operation. The murmur and symptoms then completely disappeared, and the patient remained entirely well for one and a half years after surgery. The final, complete and permanent occlusion of the patent ductus arteriosus was thought to have been brought

newborn infants with pulmonary stenosis or atresia are to be saved

As to indications, Blalock and Taussig are of the opinion that the types of abnormalities that should be benefited by the operation described are the tetralogy of Fallot and pulmonary atresia, with or without dextroposition of the aorta and with or without defective development of the right ventricle. Other abnormalities likely to be benefited are a truncus arteriosus with bronchial arteries and a single ventricle with a rudimentary outlet chamber in which the pulmonary artery is diminutive in size. The operation is indicated only when there is clinical and radiologic evidence of a decrease in the pulmonary blood flow.

They believe that the operation is not indicated in cases of complete transposition of the great vessels or in the tetralogy of Fallot of so-called "Eisenmenger type," and probably not in aortic atresia. It should not be performed when studies reveal a prominent pulmonary conus or pulsations at the hilum of the lungs.

#### COARCTATION OF THE AORTA

Crafoord and Nylin<sup>5</sup> have recently reported 2 cases of coarctation of the aorta that were cured by surgical means. Apparently these operations, which were performed in October, 1944, are the first successful ones to be done for this lesion in man. Blalock and Park,<sup>4</sup> however, had already described a method of by-passing the coarctation, which they had carried out successfully in experimental animals.

Because Crafoord had demonstrated that the flow of blood to all the organs could remain suspended for as long as twenty to twenty-five minutes without subsequent signs of organic damage, provided there was an adequate flow of blood to the brain, he took the risk of placing clamps on the aorta above and below the patent ductus arteriosus and left them in place during the time necessary to divide the ductus and suture the aorta. In one patient the aorta was thus occluded just below the origin of the left subclavian artery for twenty-seven minutes without noticeable subsequent disturbances of organs. It was on the basis of this experience in patients with patent ductus arteriosus that Crafoord conceived his operation for coarctation of the aorta, and because of the relatively bad prognosis in these cases he felt justified in making an attempt at surgical treatment. Excerpts from Crafoord's description of his operation follow:

In both patients, the aorta showed conical narrowing from the origin of the subclavian artery, and the conical constriction between the coarctation and the point of departure of the subclavian artery was much longer in the first case [a small boy] than in the second. Clamp forceps were then attached to the aorta just below the point of origin of the subclavian artery, as well as at a point as far away as possible from the first pair of aortic intercostal arteries. Small clamp forceps were then placed on all the branches arising from the aorta between the two forceps on the main trunk of the aorta. Resection

of the aorta, taking in the most constricted segment was then carried out. On the peripheral side, the incision through the aorta was made in a plane at right angles to the long axis of the aorta, 2 mm proximal to the point of origin of the first pair of intercostal arteries. Centrally, the place of incision was placed at an angle of about 45° in relation to the long axis of the aorta, owing to the fact that the lumen here was narrower than on the peripheral aspect, and about 1 cm away from the area of greatest constriction. In this way, two lumens with circumferences to fit one another were obtained. A typical Carrel aorta suture was then made. First, three interrupted sutures were placed at equal distances from each other, and then running silk sutures were sewn between the interrupted sutures, each stitch being drawn up separately to secure adequate tautness.

When the forceps were removed, it was found that an ideal artery suture with no leaks had been achieved.

The patients were both in excellent health when examined in March, 1945.

Crafoord and Nylin consider it remarkable that in both cases normal conditions as regards the blood pressure were re-established. In both the blood pressure in the legs was a little higher than that in the arms, and no true hypertension was present. They believe that this postoperative effect is in favor of the mechanical theory of hypertension in coarctation.

Working independently, Gross and Hufnagel<sup>6</sup> evolved an almost identical technic on dogs, and operated on two patients in June and July, 1945. The first patient, a six-year-old child, died when the clamps were removed from the aorta, the heart going into uncontrollable dilatation as the result of the sudden opening of the enormous vascular bed. The second patient, a twelve-year-old girl, survived the operation and was discharged in a satisfactory condition on the nineteenth postoperative day. In this case the clamps were gradually released over a ten-minute period. In view of their experience in their first case, the authors stress the importance of the slow removal of the aortic clamps.

Alexander and Byron<sup>7</sup> report the successful removal of an aneurysm of the thoracic aorta. This is apparently the first time that an aneurysm of the thoracic or abdominal aorta has been successfully removed or that the thoracic aorta has been successfully ligated. The patient, a nineteen-year-old student, showed a nonpulsating mass in the left side of the mediastinum, mild hypertension and a well established collateral circulation. A provisional diagnosis of aortic coarctation on the basis of extrinsic pressure by a neoplasm—probably a neurofibroma—was made, and thoracotomy was performed. At operation a thin-walled saccular aneurysm of the upper descending aorta was exposed in the costovertebral gutter. Its upper pole was 5 cm inferior to the left subclavian artery, and its attachment to the aorta was 7.5 cm long. The aorta appeared to be slightly constricted at its junction with the upper end of the aneurysm. Since the thin-walled aneurysm was in danger of rupture and since the collateral circulation appeared to be adequate, resection of the aneurysm



lower liver margin centrally, where the dye was not absorbed. The liver abscess was drained on the thirty-third hospital day. Abundant colon bacilli were cultured from the fluid.

Postoperatively the patient had a low-grade fever and frequently required oxygen. On the eighth hospital day an x-ray film of the chest was considerably changed, showing multiple rounded indefinite areas of increased density throughout both lungs. The appearance of the right lower lobe was unchanged. Twenty days postoperatively, after the temperature had been normal for five days, the patient was discharged to a nursing home.

*Second admission* (two months later). After discharge the patient was bedridden and continued to have a cough, dyspnea and a chronic draining wound in the upper abdomen. Two days before readmission the cough increased and there was an exacerbation of fever, with chills and headache.

The patient was moribund on admission. The findings were altered from the previous ones only in degree of severity. Rales and rhonchi were heard over both lung fields. The process seen in the x-ray film of the chest had moderately increased. The foci of increased density were connected by a network of increased densities, which were somewhat beaded and irregularly distributed. Death occurred on the third hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR. CARROLL C. MILLER. This case presents the aspects of a picture puzzle of three pieces, which have to be fitted in proper relation to one another to explain the final outcome. These three pieces are the appendix abscess, resulting from a ruptured appendix, the lung abscesses and the liver abscess. It seems to me that the important feature is the sequence of events, provided that we can demonstrate a logical sequence. In the first place, I believe that there was nothing in this case that could be considered specific, that is, I do not believe that we are dealing with a specific infection. The mention of a liver abscess makes one think of amebic abscess or echinococcal disease of the liver, both of which can cause complications such as those that occurred in this case. In a man of this age we particularly think of carcinoma or malignant disease, and malignant disease in the lung or liver is frequently masked by infection. There is nothing in this man's history, however, that suggests malignant disease, although, of course, it may have been present. It is true that there was a loss of 71 pounds in weight, but after all, this man had a history, going back over a year, of chronic sepsis, and patients with this degree of chronic sepsis often lose weight. I believe that the weight loss can be explained on that basis.

Let us first consider the appendix abscess. These days we see, fortunately, few cases of late complications of appendix abscess. Whether this is due to a better handling of acute appendicitis and rup-

tured appendix or to chemotherapy, one cannot definitely say, it probably depends on both to a certain degree. The story of appendix abscess followed in a short space of time by chills, sweating, high fever and pain in the right lower chest make me believe that there was a spreading infection from the region of the appendix or cecum. Pylephlebitis, with a spread of the infection through the veins of the portal system into the liver and the subsequent formation of multiple liver abscesses, would explain the clinical signs and symptoms.

So far as the lung abscesses are concerned, there are two possible explanations. One, which is attractive, is that since this operation was for an acute ruptured appendix it undoubtedly was an emergency procedure. We do not know the details of the operation, what anesthesia was used or what complications were associated with the immediate operative or postoperative situation, but it is possible that material was aspirated from the stomach — that is, vomitus during induction or recovery from the anesthesia may have been aspirated into the lung, with the resultant formation of multiple lung abscesses. A good many cases of lung abscess come to this hospital in which this has been the story. Usually these abscesses start out as tiny foci of infection surrounding the aspirated material, many of them in various parts of the lungs but mostly in the lower lobes. These abscesses, particularly if they are peripheral, cause pleuritic reaction with effusion and eventual contamination of the pleural cavity, with the formation of empyema. So the empyema that was found and drained may be explained on the basis of an abscess going out from the central part of the lung to the periphery. That is one direction for the train of events. Another direction, which is not infrequent, is that in a cephalad direction that is, the infection in the abdomen may have gone up under the diaphragm, perforated the diaphragm and caused an empyema, which in turn invaded the lung. This involvement of lung tissue from without is rarer, I should say, than involvement of the pleura from within the lung parenchyma. The liver abscess, as such, might have produced the same sequence of events, breaking through the diaphragm without peritoneal involvement and causing empyema and lung changes.

I should like to speculate a minute on the matter of chemotherapy, which has some bearing on this case. The patient was given sulfonamides and penicillin following the first bout of sepsis in the chest. So far as appendix abscess is concerned, we have had varying responses with the use of sulfonamides. Both sulfadiazine and penicillin have frequently seemed beneficial in cases of peritonitis from ruptured appendix. But these drugs are notorious, of course, for affecting the gram-positive organisms and not affecting the gram-negative ones, and that is borne out by the fact that in this case colon bacilli were cultured from two sources — the

about by the cellophane. The application of cellophane is not a new maneuver, but its use under similar circumstances is worth while for the possible continuing stimulation of fibrosis within the ductus

(To be concluded)

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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#### CASE 32151

##### PRESENTATION OF CASE

**First admission.** A sixty-five-year-old railroad conductor was referred from another hospital with a diagnosis of multiple abscesses of the lung.

Eight months before admission the patient had an appendectomy, with drainage because of rupture, at a community hospital. Two weeks later an abscess in the region of the cecum was drained. This was soon followed by an episode of chills and sweating, accompanied by a high fever and pain in the right lower chest. A small amount of pus was removed from the right pleural cavity. The patient received sulfonamides and penicillin and was discharged apparently well in the seventh week. Two weeks after discharge he again developed chills and fever and was readmitted. The empyema was treated by drainage and local penicillin, and he was discharged after a four-week stay. Six weeks later he entered another hospital, again with chills and fever. There was a draining sinus in the right lower posterior chest. Injection of the sinus with lipiodol showed a multilocular abscess at the level of the right hilus, with a fistulous communication into a large bronchus. He received parenteral penicillin with improvement and was discharged after six weeks, one month before his admission to this hospital. He continued to have fever and sweats

He raised large amounts of yellow, nonodorous sputum, and three days before admission the sputum became blood streaked for the first time. There had been marked dyspnea in the latter part of his illness. During the whole course he had lost 71 pounds.

On physical examination the fistula was draining small amounts of pus. There were dullness and diminished fremitus over the lower two thirds of the right chest anteriorly and posteriorly, the breath sounds were harsh and loud, and there were scattered fine rales over this area. The heart was slightly enlarged to the left, and there were numerous extrasystoles. The liver edge was 3 cm. below the costal margin. The appendectomy scar was healed.

The temperature was 101.5°F, the pulse 72, and the respirations 24. The blood pressure was 135 systolic, 65 diastolic.

The red-cell count was 3,590,000, with 10 gm hemoglobin. The white-cell count was 30,000. The urine was normal. An x-ray film of the chest showed considerable radio-opaque material in a large cavity in the apex of the right lower lobe. There was hazy increased density throughout the rest of the lobe. The right half of the diaphragm was high and immobile.

A bilateral superficial femoral-vein ligation was performed on the second hospital day. Several unsuccessful attempts were made to aspirate the right pleural cavity. On the fifteenth hospital day, the liver was tender and there was spasm of the overlying rectus muscle. The total protein was 7.19 gm, with an albumin-globulin ratio of 0.84. The prothrombin time was 26 seconds (normal, 18 seconds). By x-ray examination the liver did not appear enlarged, and its upper outline was sharply defined. A gastrointestinal series failed to reveal any deformity of the stomach or duodenal loop. Abundant colon bacilli were cultured from the sputum. In the meantime the patient had had two attacks of substernal pain, one accompanied by dyspnea, and the temperature was spiking. Several abdominal films taken during thorotrast study showed an area of decreased density within the

abscesses throughout the lungs. We did not find a thrombophlebitis. The vein ligation was described as being prophylactic in character. Infection can, of course, spread by metastases through the venous system without producing progressive thrombosis. Although the clinical sequence seems to point to lung abscess and then liver abscess, I am inclined to think that the reverse order is more probable, the first process being in the liver and the second in the lungs.

You have already heard the bacteriologic report that colon bacilli were cultured from the sputum. When the sections came through we found microscopically an additional organism, which helped to explain the failure of response to chemotherapy. The abscesses in the lungs contained numerous actinomycotic granules. We did not find any in the liver, but I presume that the process there was of the same etiology.

We did not find any lesion in the brain.

## CASE 32152

### PRESENTATION OF CASE

A twenty-one-year-old woman, a switchboard operator, entered the hospital complaining of severe headaches.

Four or five years before admission, she noticed the onset of diplopia. At first this condition was corrected by prismatic glasses, but it grew progressively worse, requiring frequent change of lenses, and one year before admission the diplopia persisted in spite of glasses. Approximately concomitant with the onset of the diplopia, the patient began to have "cramps" in the right hand. These were accompanied by a cold, numb feeling sometimes limited to the fingers and sometimes involving the entire hand. During these attacks the hand felt "frozen" in whatever position it had occupied at the onset, it did not tingle or feel numb. The right leg was never affected, and there was no disturbance of speech. One year before admission the patient began to have paroxysmal attacks of sharp stabbing pains distributed symmetrically over both cheek bones and sides of the nose but never involving the supraorbital regions, jaw, teeth or gums. These attacks occurred three to four times a day and lasted two to three minutes. They were accompanied by a cold, numb feeling having the same distribution as the pain but persisting constantly for about a week, during which the attacks of pain occurred. Then both pain and numbness subsided, to recur again for one-week periods once or twice a month. Six months before admission, the attacks of pain in the face subsided but there was an increase in the frequency and intensity of the mild headaches that she had been having occasionally ever since an illness, thought to have been undulant fever, at the age of seven.

They became severe, stabbing and throbbing in character, extending diffusely over the head but occasionally becoming more marked over the temporal and occipital regions bilaterally. They often awakened her in the early morning, gradually fading in severity after two or three hours. The onset was usually accompanied by nausea, which was sometimes followed in about half an hour by vomiting. Occasionally the patient experienced a momentary "blackout" when she stood up during one of the severe headaches, but she never lost consciousness for more than a few seconds. She also complained of severe blurring of vision during the headaches. These attacks occurred about once or twice a week without apparent precipitating factors and did not respond to any form of treatment. During the six months before admission they did not increase in frequency but gradually became severer, lasting up to six hours and then gradually fading throughout the day.

The past history and family history were non-contributory.

Examination revealed a well developed and well nourished girl in no acute distress. There was papilledema of 2 or 3 diopters in the right eye, and 1 diopter in the left. The pupils were equal, being 4 mm in diameter, and reacted normally to light and distance. There were convergent strabismus of the right eye and homonymous diplopia, persisting even on extreme lateral gaze to the left. There was no anosmia. The corneal reflexes and sensation of the face were normal. There was no facial asymmetry or weakness. An audiogram was normal. The palate and tongue were normal. There was no unsteadiness or weakness of the arms or legs. Sensation, including postural sense and stereognosis, was normal. The arm, knee and ankle jerks were brisk and bilaterally equal. There was no Hoffmann reflex. The plantar reflexes were normal.

The temperature was 99°F, the pulse 95, and the respirations 20. The blood pressure was 120 systolic, 75 diastolic.

The urine was normal. The red-cell count was 4,400,000, the white-cell count 8700, and the hemoglobin 80 per cent. The spinal fluid, which was under a pressure equivalent to 350 mm of water, was xanthochromic and contained 30 red cells and no white cells per cubic millimeter. The total protein was 7 mg per 100 cc, and the goldsol curve and Wassermann reaction were negative.

An electroencephalogram was abnormal, with slow activity increasingly prominent posteriorly. Although there was no well defined focus, the slow activity (4 to 5 seconds) was especially prominent in the left occipital and the right posterotemporal regions.

X-ray films of the skull showed unusual prominence of the convolutional markings. Only one posterior clinoid process, thought to be the right, was seen, and that seemed to have a blunted tip.

sputum and the liver abscess. Apparently the use of sulfonamides inhibited the other organisms, so that there was a persistence of colon-bacillus infection in spite of the repeated use of penicillin and sulfonamides.

It is surprising that these abscesses of the lung were apparently not foul. This is relatively unusual, but on the basis of chemotherapeutic responses, we can assume that some of the organisms that ordinarily cause foul abscesses were killed by the chemotherapy. Blood streaking of the sputum is a finding that we see frequently in lung abscess. It is not necessarily a sign of infarction or of malignant disease, but we have to think about infarction and pulmonary emboli in relation to the other findings.

A point of interest to me is the reason for the superficial-vein ligation. In this hospital we are naturally highly sensitized to the matter of embolic catastrophes coming from the veins of the legs. I should be interested to know whether this ligation was done as a prophylactic measure or with the conviction that the episodes of pulmonary difficulty were secondary to thrombophlebitis of the legs. It seems that the latter was probably the case. We are not told whether clots were found in the veins, and no mention is made of the flow of blood from above. It would be of some interest in this case, because I suspect that there was a phlebitis in the abdomen above the point of ligation. In the early days of his illness this man had repeated episodes of chills, fever and chest pain. After he came to the hospital he again had episodes of pain, two of them substernal, accompanied by dyspnea, which to me suggest pulmonary infarction. Before we see the x-ray films I shall briefly mention the second admission, which simply showed an exacerbation of all the signs previously manifested, with, in addition, headache. This may have been simply a reflection of the sepsis and of the high temperature, but it is suggestive to me of the possibility of a metastatic brain abscess. The headache was not mentioned previously, and we know that the three most frequent causes of death in lung abscess are sepsis, hemorrhage and brain abscess.

May we see the x-ray films?

DR JAMES R. LINGLEY: These are the first films and show the large area of density at the right base, which in the lateral view lies posteriorly and evidently represents encapsulated fluid. The appearance of the lipiodol suggests an alveolar distribution rather than lipiodol lying in a cavity. It was stated in the record that it communicated with the bronchus on the left side. In the lateral film there is a diffuse process, even at this time, of patchy areas of density distributed throughout the lung. This is the film taken five weeks later. There is a marked advance of the process throughout the left lung. The areas of involvement are small and circumscribed, yet it is a diffuse process involving the entire lung field.

DR MILLER: Do you think that is a cavity?

DR LINGLEY: I cannot see anything that looks like a cavity except this area on the right.

DR MILLER: It is possible that that might be an advance of the diffuse linear process seen in the previous film.

DR LINGLEY: Yes.

DR MILLER: Have you the thorotrast films? They are of some interest.

DR LINGLEY: This film after thorotrast injection shows two areas of diminished radiance and rarefaction in the liver.

DR MILLER: In recapitulation, I assume that this patient had a septic phlebitis arising in the region of the cecum and involving the iliac vein on that side and perhaps spreading up the inferior vena cava, although I find no sign of caval blockage in the picture that is described. I suppose that we must also predict a pyelephlebitis to account for the liver abscess, because I do not believe that a process coming down from the lungs could have produced these multiple liver abscesses. So, although the temptation is great to ascribe the multiple lung abscesses to aspiration from the esophagus at the time of operation or shortly thereafter, I am a little more in favor of the picture's being explained on the basis of septic infarction of the lungs, arising from the right iliac vein, with metastases to the lung, and eventually from the lung to the brain to explain the possible brain abscess. The pyelephlebitis may have followed an independent route, traveling through the portal system into the liver.

#### CLINICAL DIAGNOSIS

Multiple abscesses of lung and liver

#### DR MILLER'S DIAGNOSES

Thrombophlebitis, right iliac vein  
Septic lung infarcts, with abscess formation  
Pylephlebitis  
Liver abscesses  
Brain abscess?

#### ANATOMICAL DIAGNOSES

Multiple abscesses, pericecal, hepatic and pulmonary  
Actinomycosis of lungs  
Operative wounds: appendectomy, old, drainage of empyema and lung, subdiaphragmatic and liver abscesses  
Arteriosclerosis, generalized

#### PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY: At autopsy, we found abscesses in three areas. There was a persisting abscess in the region of the cecum that had not been entirely drained. There was a large abscess in the liver, which at the time of autopsy appeared as a single abscess, although it may well have been multilocular in the early stages, and there were multiple

On the positive side of the balance there are yet other reasons for thinking that the ventriculogram is a correct portrayal of the situation. The headache was periodic, but its periodicity was not without system. We note that the patient was frequently awakened by headache, but that on assuming the erect posture it subsided, at first within an hour or two and somewhat later in the disease only after five or six hours of being out of bed. This suggests that the headaches were due to intermittent obstructions to the flow of cerebrospinal fluid that were related to changes in posture. A mass situated in the third ventricle is certainly in a strategic location for producing such a ball-valve action on the circulating fluid. Supporting this as a possibility is the finding that the spinal fluid was yellow and contained a little blood.

DR. KUBIK: The lumbar puncture was done after the ventriculogram.

DR. HEUSNER: My abstract says that the spinal fluid was xanthochromic.

DR. KUBIK: I am sorry about that.

DR. HEUSNER: We cannot, then, call on xanthochromia as a means of supporting the possibility that something was protruding into the ventricular system, but that is a finding we have come to recognize as likely when some abnormal tissue is lying in a subependymal position or actually within a ventricle.

But there are other reasons for accepting the ventriculographic suggestion of a mass in the posterior portion of the third ventricle. If we are to explain the symptomatology on the basis of a single lesion, that lesion must be in close proximity to the central sensory components subserving both sides of the body, for although it is true that the pains began in the right hand, later in the disease they appeared bilaterally over the face. Certainly a mass in the third ventricle, the walls of which are composed in part of the thalamus, important sensory substations, would be favorably situated to effect bilateral pain. I do not know how a lesion in that position actually produces pain, yet the clinical description of this patient's discomfort is to me not unlike what we sometimes see following a thrombosis involving the thalamus. For these several reasons, then, I am going to accept the ventriculogram as having demonstrated the presence of a space-occupying something in the posterior portion of the third ventricle.

This is a long history. What slowly growing things occur in this region? Accumulated experience shows that practically everything from granulomas and parasitic cysts through various tumors have been found in this location. But since we have nothing to suggest a granuloma or parasitic cyst, I am going to confine my comments to the reasonable statistical possibilities, namely, the tumors

Of the tumors that come to occupy the third ventricle, the great majority arise outside the ventricle and eventually extend into it, the minority are primary intraventricular tumors. Of the tumors that arise outside and eventually gain access to this ventricle, the most frequent one is, I think, the Rathke-pouch tumor. In this case I do not believe that we need seriously consider such a lesion. The characteristic visual-field changes and suprasellar calcification are wanting, and what is more significant, the anterior portion of the third ventricle was visualized. Such a tumor should obstruct the anterior portion of this cavity before the posterior part is obliterated. On similar grounds I shall eliminate the occasional pituitary tumor that bursts its bounds, reaches the third ventricle and produces a hydrocephalus, the visual-field changes characteristic of that lesion are missing, the sella is not ballooned, and the anterior portion of the third ventricle was visualized. There is, however, a relatively frequent group of tumors arising in the pineal body near the back of the roof of the third ventricle. Such tumors not infrequently extend downward and come to fill a part or even all of this ventricle. I see no way of ruling out such a growth in this case, even though the patient did not show the large fixed pupils and impairment of upward gaze that are sometimes produced by such a mass pressing on the tectum of the midbrain.

There are two tumors that frequently arise within the third ventricle, if any third ventricular tumor may be said to be frequent—colloid cyst and papilloma of the choroid plexus. I see no way of definitely ruling out either of these. Yet, in the great majority of cases colloid cysts arise from the anterior portion of the roof of this ventricle,<sup>1</sup> and since that portion of this ventricle was visualized I should not expect this patient to harbor a colloid cyst. In other words, it seems as if this patient's mass originated more posteriorly than is usual for colloid cyst. Papilloma of the choroid plexus, on the other hand, is apt to arise from the posterior portion of the roof, and it is notorious that tumors arising in that region may go for a long time before they give rise to serious obstructive or neighborhood symptoms. So, it appears to me that the likeliest statistical possibilities in this case are pinealoma and papilloma of the choroid plexus.

The position of a mass occupying the third ventricle is of extreme importance to the surgeon, because if he can be certain of this his operative approach is likely to be successful. In a case of this type the surgeon is primarily interested in knowing whether the tumor is more accessible from the back or from the front of the ventricle. The air studies provide the answer: the tumor was more posterior than anterior.

My diagnoses are internal hydrocephalus, involving the lateral ventricles and the anterior portion of the third ventricle, and a tumor occupying the

A ventriculogram showed both lateral ventricles well filled and normal in shape and position, but they appeared to be somewhat enlarged. No air was seen in the third ventricle, aqueduct or fourth ventricle. The foramen of Munro was visualized.

An operation was performed.

### DIFFERENTIAL DIAGNOSIS

DR A PRICE HEUSNER\* Before undertaking an analysis of this case I should like to ask two questions. Are the results of a visual-field examination available? Is the abstract correct in reporting that the spinal-fluid total protein was 7 mg per 100 cc?

DR CHARLES S KUBIK That was ventricular fluid. The visual fields were normal except for large blind spots resulting from the papilledema.

DR HEUSNER But nothing striking.

DR KUBIK No.

DR HEUSNER We are asked to consider a twenty-one-year-old woman who was forced to enter the hospital because of increasing severity and frequency of headaches, which she had had for as many as twelve or fourteen years. It is quite difficult, I believe, to make sure whether these headaches were a part of the present illness or whether she had them from some other cause. In any event she had had headaches, and they finally forced her to the hospital, with nausea and vomiting. Five years before admission she noted the onset of what became a persistent diplopia, and at about the same time she began to suffer paroxysmal painful subjective sensations in the right hand. The latter apparently subsided after an unstated length of time, but some four years later they were followed by the development of similar paroxysmal sensations that occurred in a butterfly distribution over the face—in other words, they were bilateral.

The various examinations done at the time of admission give us unequivocal evidence of the existence of an elevated intracranial pressure: the disks were choked, the plain x-ray films showed convolutional atrophy, and the spinal tap revealed a pressure equivalent to 350 mm of water. On the other hand, this bizarre symptomatology, extending back at least five and perhaps as many as fourteen years, did not leave in its wake anything that I can regard as a definitely localizing neurologic sign. On admission she had an internal strabismus of the right eye, which I take to be evidence of palsy of the right abducens nerve and adequate cause for the diplopia that she had experienced for several years. The note that the diplopia persisted even in extreme left lateral gaze permits of more than one neurologic interpretation. It might mean a beginning palsy of the left abducens nerve or a disturbance of the mechanism, situated high in the mid-brain, that regulates conjugate movements of the eyes. Because no one of these signs may be depended on for localization when it occurs in con-

junction with an elevated intracranial pressure, it is not surprising that a ventriculogram was made. It would be helpful to see these films at this point and also the plain x-ray film of the skull, which was described as showing convolutional atrophy.

DR JAMES R LINGLEY These are the plain films showing the convolutional atrophy, as well as some thinning of the posterior clinoid process, but no definitely localizing signs.

DR HEUSNER The sella is not ballooned?

DR LINGLEY No, I should say that it is normal in size.

In the ventriculogram there is dilatation of both lateral ventricles, and you can trace air down into the anterior portion of the third ventricle. This small quantity of air in the anterior portion of the third ventricle outlines the anterior border of a mass that fills the posterior part of the ventricle. In the lateral view you can also see the mass projecting up into the floor of the lateral ventricles, more marked on the left side than on the right. The x-ray findings therefore indicate a mass filling the posterior portion of the third ventricle and projecting up into the floor of the left lateral ventricle.

DR HEUSNER There is therefore objective evidence that air failed to reach the body and the posterior portion of the third ventricle. This suggests the presence of a mass in the back end of the third ventricle, but before accepting this as an absolute certainty it would be wise to inquire whether the suggested localization is clinically reasonable. Although it is true that the ventriculogram remains the neurosurgeon's most reliable single localizing adjunct, it is not a method without caprice. Occasionally, even in the most experienced hands, failure to visualize some portion of the ventricular system does not mean that that portion of the system is occupied by a pathologic mass. Let us, then, harken back to the symptomatology and see if the localization suggested by this ventriculogram is clinically reasonable.

If we consider the over-all picture of a twenty-one-year-old woman with choked disks but without localizing signs, one of the first lesions we should think of is a neoplasm in the posterior fossa. We have, then, to ask ourselves whether it is more reasonable to expect a lesion in the posterior fossa or one in the posterior portion of the third ventricle, as suggested by the ventriculogram.

There are numerous reasons for accepting the ventriculographic localization in this case. The history and neurologic signs are not those of posterior-fossa disease. None of the cranial nerves in that region have suffered, and there are no signs or symptoms, such as ataxia, dysmetria and nystagmus, suggesting disorder of the cerebellum itself. Further, in posterior-fossa tumors the entire third ventricle shares in the hydrocephalic enlargement, a circumstance affording the best possible chance for filling that cavity with air.

\*Associate surgeon for neurosurgery, Boston City Hospital

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THE INADEQUACIES OF MEDICAL CARE

I GENERAL CONSIDERATIONS

WHAT is wrong with the practice of medicine? As long ago as 1927 the Committee on the Costs of Medical Care was organized by a group of leading physicians, public-health authorities and economists to solve the problem — “the delivery of adequate scientific medical service to all the people, rich and poor, at a cost which can be reasonably met by them in their respective stations of life ” Although extensive majority and minority reports were rendered at that time, matters have little improved, and the point has finally been reached at which compulsory health insurance is advocated by President Truman, certain congressmen and others as the *only* means by which the health of the Nation

can be assured Such a scheme or any other plan for distributing the costs of medical care concerns merely one of the many factors that contribute to the health of the Nation Similarly, the art and the science of medicine, which admittedly are developed in the United States to a degree that is unsurpassed in any other country, comprise another single factor In other words, adequate and proper medical care for all largely depends on various socioeconomic factors with which the majority of physicians have had little experience and over which they have little control

In any broad concept of matters pertaining to national health many factors have an equal, if not greater, influence than has medical care These include good wages, a high standard of living, adequate housing and transportation facilities and a public well educated concerning proper diets, methods of preventive medicine and means of obtaining medical care Although the lack of one or more of these factors renders the success of any system of medical care questionable, if not impossible, they have received little consideration by those clamoring for compulsory health insurance Such matters, of course, are not true responsibilities of the medical profession, except for the fact that physicians might well play more of a role than they have in the past in matters of lay education On the other hand, many inadequacies pertaining directly or indirectly to medical care exist, and the refusal to recognize and admit these faults has done much to lead to the position in which, unfortunately, the medical profession now finds itself

In the last fifty years, the science of medicine has made tremendous progress, possibly at a sacrifice to the art The “family doctor” as he existed in the nineteenth century is a person of the past, since it has become impossible for any one physician to care properly for *all* the aches and pains of his clientele Although the man in general practice will undoubtedly continue to comprise the bulwark of the medical profession, being just as essential to it as was the infantry to the modern army, this advance in the science of medicine frequently demands elaborate diagnostic aids and the advice and technical skill of the so-called “specialist ” In cases of serious illness, it has put a premium on hospitaliza-

posterior portion of the third ventricle — either a pinealoma or a papilloma of the choroid plexus

DR. AUGUSTUS ROSE How do you explain the diplopia?

DR. HEUSNER To explain that I have to fall back on the experience of others. The tumors that occur in this region are rare. I have seen very few of them, but the symptoms in 2 of Dandy's<sup>1</sup> 15 cases of primary intraventricular tumor began with diplopia.

DR. ROSE You think that it is a sixth-nerve palsy?

DR. HEUSNER I do not know.

DR. ROSE I do not know either.

DR. JAMES B. AYER Does not a pineal tumor usually show in a ventriculogram by the time that it has done this much damage?

DR. HEUSNER I believe so, and I also believe that Dr. Lingley pointed out a fullness extending up into the lateral ventricle in one of the projections.

I am glad that no one has asked me to explain the pain in this patient's arm or face, but again falling back on the experience of others, I find that similar pains have been observed, although not in



FIGURE 1

a butterfly distribution. Those who have tried to formulate clinical syndromes of third ventricular disease have included among them a so-called "thalamic syndrome" resulting from tumors in this region and characterized by spontaneous, often paroxysmal, pain.<sup>2,3</sup>

In my abstract the spinal fluid was said to be yellow. Had the tap been done before the ventriculogram, I should have favored a papilloma of the choroid plexus ahead of pinealoma, but without that, I assume that the spinal fluid was initially clear. On statistical grounds I guess that a growth arising in the pineal is the likelier.

DR. WILLIAM H. SWEET The extreme duration of symptoms, as suggested by the convolutional atrophy of the skull, might also lead to the diagnostic possibility of an epidermoid tumor, since that is the slowest growing of the congenital-rest tumors that are seen in the third ventricle.

DR. KUBIK Would you like to add anything more about the operative findings?

DR. SWEET On the basis of the extreme duration of symptoms it appeared to me that a colloid cyst or an epidermoid tumor were the likeliest diagnoses. I searched a long time and finally found a small colloid cyst involving the third ventricle. I was not able to find any evidence that the lateral ventricle on either side had been encroached on by a space-taking mass and had a rather difficult task to get between the internal cerebral veins without hemorrhage. This was eventually achieved, and a small yellowish mass encountered, which was readily removable, it was not attached to any significant amount of the roof of the third ventricle, and after aspiration of the viscous fluid content, the collapsed capsule was readily lifted out.

DR. KUBIK How large would you say that it was?

DR. SWEET About 10 or 15 cm. in diameter.

DR. KUBIK And the subsequent course?

DR. SWEET The patient was apathetic postoperatively for a week or two. After two or three weeks she began to behave normally, and when heard from three months postoperatively she had no complaints and was leading an active life.

#### CLINICAL DIAGNOSIS

Colloid cyst of third ventricle?

Epidermoid tumor of third ventricle?

#### DR. HEUSNER'S DIAGNOSES

Internal hydrocephalus, involving lateral ventricles and anterior portion of third ventricle.

Tumor occupying posterior portion of third ventricle (? pinealoma or papilloma of choroid plexus).

#### ANATOMICAL DIAGNOSIS

Colloid cyst of third ventricle.

#### PATHOLOGICAL DISCUSSION

DR. KUBIK The mass removed by Dr. Sweet, as he has already stated, was a colloid cyst of the third ventricle. A similar case has been reported.<sup>4</sup> The patient was a forty-nine-year-old woman who had been having headaches for one year and became comatose a week before entering the hospital. There were no focal signs. The cyst, measuring about 1 cm. in diameter, was attached to the roof of the third ventricle between the optic thalami. It is possible, I suppose, that its relation to the optic thalami accounted for pain or paresthesia, as suggested by Dr. Heusner. The section shows a thin cyst wall lined with columnar ciliated epithelium (Fig. 1). These cysts, which are benign and removable, are thought to originate from vestigial cells of the paraphysis.

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## THE INADEQUACIES OF MEDICAL CARE

### I. GENERAL CONSIDERATIONS

WHAT is wrong with the practice of medicine? As long ago as 1927 the Committee on the Costs of Medical Care was organized by a group of leading physicians, public-health authorities and economists to solve the problem — "the delivery of adequate scientific medical service to all the people, rich and poor, at a cost which can be reasonably met by them in their respective stations of life." Although extensive majority and minority reports were rendered at that time, matters have little improved, and the point has finally been reached at which compulsory health insurance is advocated by President Truman, certain congressmen and others as the *only* means by which the health of the Nation

can be assured. Such a scheme or any other plan for distributing the costs of medical care concerns merely one of the many factors that contribute to the health of the Nation. Similarly, the art and the science of medicine, which admittedly are developed in the United States to a degree that is unsurpassed in any other country, comprise another single factor. In other words, adequate and proper medical care for all largely depends on various socioeconomic factors with which the majority of physicians have had little experience and over which they have little control.

In any broad concept of matters pertaining to national health many factors have an equal, if not greater, influence than has medical care. These include good wages, a high standard of living, adequate housing and transportation facilities and a public well educated concerning proper diets, methods of preventive medicine and means of obtaining medical care. Although the lack of one or more of these factors renders the success of any system of medical care questionable, if not impossible, they have received little consideration by those clamoring for compulsory health insurance. Such matters, of course, are not true responsibilities of the medical profession, except for the fact that physicians might well play more of a role than they have in the past in matters of lay education. On the other hand, many inadequacies pertaining directly or indirectly to medical care exist, and the refusal to recognize and admit these faults has done much to lead to the position in which, unfortunately, the medical profession now finds itself.

In the last fifty years, the science of medicine has made tremendous progress, possibly at a sacrifice to the art. The "family doctor" as he existed in the nineteenth century is a person of the past, since it has become impossible for any one physician to care properly for *all* the aches and pains of his clientele. Although the man in general practice will undoubtedly continue to comprise the bulwark of the medical profession, being just as essential to it as was the infantry to the modern army, this advance in the science of medicine frequently demands elaborate diagnostic aids and the advice and technical skill of the so-called "specialist." In cases of serious illness, it has put a premium on hospitaliza-

tion and all that goes with it. Many persons, however, are unable to obtain admission to a hospital, either because the facility is nonexistent or because beds are unavailable, and combined with this lack or scarcity of hospital facilities is the apparent inability of the medical profession to adapt itself to the changing practice of medicine, either wishfully or because of ignorance of the basic factors that are involved.

The subsequent editorials of this series will point out what appear to be the present-day inadequacies of medical care—as they concern its distribution and cost, its quality and the various adjuncts that are closely associated with, if not essential to, its successful accomplishment—and to hazard a guess concerning what must be done if the health of the Nation is to be improved.

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## PENICILLIN AND SYPHILIS

### A SECOND WARNING

IN A previous editorial in the *Journal*,<sup>1</sup> attention was called to the known fact that syphilis may lie dormant for long periods and later produce clinical effects or be transmitted to a second generation. Emphasis was laid on the importance of serologic follow-ups over a period of years in all persons who have been treated with penicillin for syphilis so that the exact potentialities and end-results of this method may be fully determined. In particular, returning veterans who had been treated for syphilis were mentioned as requiring this follow-up, because in many of them, early in the experimental period of this form of therapy, relatively small doses of penicillin were used. The same, however, may also be said of civilians—including those treated more recently with various combinations of penicillin with arsenicals and bismuths.

Of equal and perhaps greater importance is the need to search for serologic and clinical evidence of syphilis in patients who have been treated with penicillin for gonorrhea. The fact that gonorrhea and syphilis are frequently acquired at the same time but have different incubation periods, as well as the nature of the effect of small doses of penicillin

on the early manifestations of these two infections, renders the masking of the early manifestations of syphilis a definite possibility. Thus, the incubation period of gonorrhea is usually three to five days and only rarely more than a week, and its manifestations are usually obvious enough to the patient so that medical treatment is sought. As little as 100,000 units given in four or five intramuscular doses over a period of six to nine hours or a single dose of 200,000 or 300,000 units in a beeswax-peanut oil mixture produces complete cures in the great majority of cases. The incubation period of syphilis, on the other hand, is usually about three or four weeks and may be much longer. Treatment for gonorrhea may, therefore, be given some time before the primary syphilitic lesion appears.

Leifer and Martin<sup>2</sup> have recently reported on 15 cases of simultaneous infections from their own experience and from the literature. They very properly point out that for various reasons penicillin treatment of gonorrhea may be undertaken when primary syphilis is already present but overlooked or ignored. For example, a primary lesion may be missed because of its unusual location, it may be concealed by inflammatory phimosis, it may be regarded as an unimportant lesion or the diagnosis may seemingly be excluded by one or more negative dark-field examinations or by negative serologic tests for syphilis. In the earliest studies on the penicillin treatment of syphilis it was shown by Mahoney, Arnold and Harris<sup>3</sup> that the primary lesion undergoes rapid changes within a few hours after treatment is started. With doses of 25,000 units every four hours, spirochetes disappear from the lesion, as shown by dark-field preparations, within sixteen hours or even earlier. There may also be clinical symptoms within the first eight hours that suggest a therapeutic effect. These include fever, pain at the site of the lesion and enlargement or tenderness of the regional lymph nodes, occasionally a brief rash resembling that of secondary syphilis appears.

Leifer and Martin also point out that the small doses of penicillin that are used in the treatment of gonorrhea may conceivably bring about a cure of a coincidental early syphilitic infection in rare cases. It is likelier, however, that a chancre will appear perhaps after a prolonged period of incubation. It

may be expected that treatment in the primary stages of syphilis will heal the lesion prematurely, after which it may either recur, the disease may be rendered asymptomatic or a secondary eruption may appear. In addition, a Herxheimer reaction may be evoked in the course of treatment, either at that time or on some subsequent occasion when penicillin is given. In the cases that they studied, the diagnosis of syphilis was proved in every instance either by demonstration of spirochetes in the lesions or by repeated positive serologic tests in less than ninety days after penicillin had been administered. On the basis of their observations these authors recommend that all patients treated with small doses of penicillin for gonorrhea<sup>2</sup> should have clinical and serologic observations for a period of three months.

Another interesting feature of penicillin treatment may be anticipated and has probably already been observed by some physicians. Many persons with latent or manifest syphilis undoubtedly receive penicillin therapy for other conditions, the drug being given for a brief course while the patient is acutely ill or in larger doses over longer periods for the treatment of such conditions as septic wounds, osteomyelitis and subacute bacterial endocarditis. In any event, an early febrile reaction may occur during the first few hours of penicillin treatment, and this may be accompanied by symptoms of various severity which may be easily overlooked or misinterpreted. A rise in fever, a chill or a headache may be considered as a phase of the infection that is being treated, and a rash may be considered as a sensitivity reaction to penicillin, whereas actually these signs and symptoms are manifestations of a Herxheimer reaction. Physicians should be on the alert for these types of reactions and should obtain blood for serologic tests for syphilis at such a time. Positive results may be reported in occasional cases in which previous tests have been negative or in which the diagnosis of syphilis has not otherwise been suspected.

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## OBITUARY

## SAMUEL BAYARD WOODWARD

1853-1946

Samuel Bayard Woodward, the son of Samuel Woodward, a merchant of Worcester, Massachusetts, and his wife, Elizabeth Rogers Treadwell Woodward, was born August 24, 1853. On his father's side he was a descendant of Dr. Henry Woodward, who settled in Dorchester in 1653 and carried on the practice of medicine there. On his mother's side, the members of Thomas Treadwell's family were fellow passengers on the ship with Dr. Henry Woodward. They settled in Ipswich.

Another Woodward, Dr. Samuel, lived in Torrington, Connecticut, and Dr. Samuel Bayard Woodward I, grandfather of the subject of this obituary, settled in Weathersfield, Connecticut, later moving to Worcester, Massachusetts. He was the first superintendent of the Worcester Lunatic Hospital.

His grandson, after an adequate premedical preparation, including an A.B. degree from Harvard College, entered Harvard Medical School and graduated as one of the honor men of his class. He then was appointed house officer at the Boston City Hospital, where he won the confidence of the visiting staff and his associates. Having decided to prepare himself for the greatest possible usefulness in dealing with the problems of disease, he studied abroad for three years, visiting the hospitals of Dublin, London, Heidelberg, Vienna, Strasbourg and Paris.

On his return to his native city he immediately sought the advice of the older doctors and decided to settle in Worcester. He joined the Massachusetts Medical Society in 1877 and immediately became active in the affairs of the Worcester District Medical Society, being elected treasurer in 1886 and president in 1902. His election to the Council of the state society followed the next year. These positions, together with his activity on committees, were preludes to his election as president of the state society in 1916. Since his administration of the affairs of the Society was noteworthy, he was asked to accept the honor of a three-year term, a distinction not previously conferred since 1862.

His service during these years was especially arduous because of the threat leading up to and the declaration of war in 1917, which necessitated raising the required medical personnel for the Army and Navy, together with frequent meetings of legislative committees. Health insurance was being considered throughout the country at that time, and the Council appointed a committee to study the subject, but no reports were rendered and many years elapsed before this matter was brought up.

again and a successful plan adopted. Workmen's compensation also engaged the attention of the Society during the war years, and the law relating to this important economic matter was put into workable form after much study and many amendments.

By reason of Dr. Woodward's reputation for executive ability, he was requested by many financial institutions to help carry on the work of their corporations. In 1885 he united with others in the incorporation of one of the large savings banks of the state, later becoming its president. The success of this bank led to the development of a national bank and other savings banks in Worcester, with his name on the list of officers.

These activities led in turn to other important positions in a great variety of active corporations engaged in business, philanthropy, education and sociologic activities to the extent of thirty or more units to which he gave his time in meetings and important decisions, a most remarkable combination of responsibilities for a busy doctor to assume. His friends became concerned because of the likelihood of his inability to carry on so much without a breakdown, but his physical and mental energy seemed adequate for the demands made on his time and strength, and he continued this routine of attending innumerable meetings throughout the thirty or more years of his professional work and never relegated his medical interests to second place.

In addition to his hospital appointments, he especially enjoyed the position of trustee of the Worcester State Hospital, to which he gave much time, only to resign in 1914 under protest because of the change made to a paid board of three in place of the former unpaid board. He was able a few years later to have this serious mistake corrected.

His long contest before legislative committees to prevent the repeal of the law requiring the vaccination of school children covered many successive years. His voluminous papers, copies of addresses and many letters used in his arguments during this campaign were deposited in the Boston Medical Library several years ago.

These brief references to the work done and positions occupied by this public-spirited physician, who served his community, as well as his state, in many effective ways set a pattern of living that might well inspire others of equal strength and understanding to plan a routine of equal service to those who are in need of assistance and guidance, especially those who are victims of misfortune.

Two legacies in Dr. Woodward's will demonstrate his affirmation that medicine was his major interest. One is a large bequest to the Worcester District Medical Society for the creation or acquisition of a building in which meetings can be held and all the functions of the society can be efficiently carried on. The second is a grant to the Massachusetts Medical Society of an amount to augment the provisions of

the Cotting Fund, established by a former active and devoted member for the purpose of entertaining those members of the Council in attendance at its meetings, a wise and effective provision designed to promote harmony among the members.

Dr. Woodward has in a great variety of ways left with us a memory of his ideals and successes that should encourage emulation.

W P B

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

COUSENS — Nicholas W. Cousens, M.D., of Waltham, died March 19. He was in his eighty-second year.

Dr. Cousens received his degree from the Medical Faculty of Trinity University, Toronto, in 1891.

His widow and three children survive.

SULLIVAN — Cornelius A. Sullivan, M.D., of Braintree, died March 19. He was in his sixty-seventh year.

Dr. Sullivan received his degree from Tufts College Medical School in 1904. He was past president of Norfolk South District Medical Society, medical consultant, Norfolk County Hospital, staff member of South Shore Hospital, South Weymouth, and Braintree school physician for many years. He had been associate medical examiner for Norfolk County for twenty-two years. He was a fellow of the American Medical Association.

His widow, a son and four daughters survive.

### NOTICES

#### ANNOUNCEMENTS

Dr. Julius Abramson announces his return from military service and the opening of his office for the practice of cardiology at 127 Bay State Road, Boston.

Drs. J. Englebert Dunphy and Stanley O. Hoerr announce the resumption of the practice of surgery at 721 Huntington Avenue, Boston, and 1101 Beacon Street, Brookline.

Dr. George H. R. Gosman announces that Dr. Joseph W. Tiede, having recently returned from active service, will be associated with him in practice at 121 Water Street, Boston.

Dr. Henry W. Hudson announces his return to the practice of surgery with offices at 1672 Beacon Street, Waban, and 1101 Beacon Street, Brookline.

Dr. Bernard M. Jacobson has returned from Naval duty and will resume the practice of internal medicine at 276 Commonwealth Avenue, Boston.

Dr. Elihu I. Lewis, having been released from active duty with the United States Navy, announces his return to the practice of internal medicine at 510 Commonwealth Avenue, Boston.

## SUFFOLK DISTRICT MEDICAL SOCIETY

The spring dinner meeting of the Suffolk District Medical Society will be held at the Harvard Club of Boston on Saturday, April 27, at 7 p.m. Representative Edith Nourse Rogers will speak on the subject "Medical Legislation in Congress for Veterans" and Dr. J. C. Harding, assistant medical director for the auxiliary services of the Veterans Administration, will speak on "Highlights in Problems Relating to the Civilian Doctor and the Medical Care of Veterans."

Members and their wives are cordially invited to attend. The tickets which are \$3.00 each must be purchased in advance by sending cash or check to the treasurer, Dr. Richard S. Eustis, 319 Longwood Avenue, Boston 15, before April 20. After this date, other members of the Massachusetts Medical Society and their wives may apply.

(Notices continued on next page)

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## CLINICAL AND LABORATORY STUDIES OF RELAPSING VIVAX MALARIA OF PACIFIC ORIGIN\*

LIEUTENANT COLONEL HARRY H GORDON, M C, A U S, COLONEL ALEXANDER MARBLE, M C, A U S,  
LIEUTENANT COLONEL STUART W LIPPINCOTT, M C, A U S,  
MAJOR WILLIAM B HESSELBROCK, S N C, A U S, AND  
CAPTAIN LESTER D ELLERBROOK, S N C, A U S

SINCE members of the armed forces have been stationed in areas in which malaria is prevalent, many of them will experience symptoms of the disease, either as delayed primary attacks or as relapses, when suppressive treatment is discontinued on their return to nonendemic areas. It seems worth while, therefore, to present a brief summary of the clinical features and laboratory findings in 808 soldiers admitted from Pacific areas to the Malaria Section of the Harmon General Hospital from August, 1943, to March, 1945. Certain of the data have been presented in greater detail in recent articles.<sup>1-4</sup>

### TYPE OF MALARIA

Although the patients came from areas in which falciparum malaria was endemic, and although many of them stated that some of their previous malarial attacks had been caused by *Plasmodium falciparum*, this organism was demonstrated in only 1 of 864 clinical attacks, and in this case it contributed to a mixed infection with *P. vivax*. This evidence strongly supports the statement that the use of quinacrine (Atabrine) in adequate doses completely cures falciparum malaria.<sup>5</sup> From the discussion that follows, it will be noted that the clinical features of vivax malaria observed in these patients differed considerably from those described in falciparum infections by Most and Meleney,<sup>6</sup> but it should be pointed out that extremely few of the patients had arrived in the United States directly from areas in which there was inadequate control of mosquitoes.

### INFECTIOUSNESS

The infectiousness of patients with clinical attacks of malaria depends on the presence of gametocytes in the peripheral blood. Thin smears were examined for gametocytes in a total of 401 attacks. In 196 (49 per cent), they showed gametocytes.

\*From the Army Service Forces Eighth Service Command, Harmon General Hospital, Longview, Texas.

In 255 attacks, treatment was not begun for approximately forty-eight hours after the onset of the relapse. In only 41 attacks (16 per cent) did blood smears taken daily or twice daily show the development of two or more gametocytes per 100 white cells, a level at which it is considered worth while to attempt to infect mosquitoes for transmission tests.<sup>†</sup> Since prompt initiation of treatment quickly eradicated parasites (Table 1), it is

TABLE 1 Effect of Quinacrine on Blood Smears and Fever

INTERVAL AFTER BEGINNING OF TREATMENT*	PERCENTAGE OF 321 PATIENTS WITH NEGATIVE SMEARS†	PERCENTAGE OF 434 PATIENTS WITH ORAL TEMPERATURES OF 99.2°F OR LESS
days		
1	33	26
2	94	71
3	99	83
4	99	91

\*Treatment of acutely ill patients was begun soon after admission to the ward but only if both a positive smear and an oral temperature of 100°F or higher were present.

†Only those patients are included who had a smear taken on each day.

obvious that there is extremely little danger of transmission of the disease if it is diagnosed promptly and if treatment is begun immediately after a positive smear is obtained. This does not in any way mitigate the need for adequate mosquito control. During a period of over one and a half years during which patients with malaria have been treated at this hospital, not a single patient has been admitted to the wards whose disease was considered to have been contracted here.

### CLINICAL FEATURES

The two essential clinical features of the disease as observed in this study were the relative mildness of the acute attack and its stubborn tendency to relapse.

†The parasite counts in these patients were made by the staff of the Laboratory of the United States Public Health Service Imported Malaria Studies. The transmission tests referred to were carried out by this group to determine whether overseas strains of malaria were transmissible by means of infected, laboratory-bred American mosquitoes. The results of this study will be reported elsewhere.<sup>7</sup>

### Characteristics of the Acute Attack

Less than 10 per cent of the patients showed any cerebral symptoms. The prompt subsidence of such symptoms with routine therapy led to the impression that these manifestations were such as would be found in any group of patients with high fever.

The infrequency of troublesome vomiting is evidenced by the fact that parenteral fluids had to be administered in less than 10 of the 864 attacks. Nausea and vomiting were present in about one fourth of the attacks, but with subsidence of the acute febrile phase under quinacrine therapy these symptoms gradually cleared.

There were prompt subsidence of fever and other symptoms and rapid disappearance of parasites from blood smears with the administration of quinacrine in customary doses of 0.2 gm every six hours for five doses, followed by 0.1 gm three times a day for six days until a total of 2.8 gm had been given. Table 1 shows that on the second day after the beginning of quinacrine therapy, 94 per cent of the patients had negative smears and 71 per cent had a maximum oral temperature of 99.2°F or less. Since a large majority of these patients had previously had several attacks of malaria, most of which had been treated with quinacrine, the prompt eradication of malarial parasites in these attacks indicated the continued effectiveness of the drug in the acute attack.

### Interval Symptoms

Although the acute attacks of malaria were relatively mild and the symptoms promptly subsided with quinacrine therapy, many of the patients complained of easy fatigability, nervousness and dyspepsia between relapses. In the majority of cases these symptoms seemed to be strongly conditioned by factors such as exposure to combat and adverse living conditions in the Pacific areas or previous personality problems. Recurrent malaria added to the patients' difficulties but was not primarily responsible for them. The patients needed much reassurance that the ultimate prognosis for the complete cure of their malaria was good, since they had returned to areas in which the chance of reinfection was slight.

### Data on Relapses

The marked tendency to relapse is indicated by the fact that of 287 patients with attacks treated with quinacrine at this hospital and followed either until a proved relapse occurred or at least sixty days had elapsed after treatment was completed, 193 (67 per cent) had relapses. As is evident in Table 2, neither the continued use of small doses of quinacrine for sixty days (compare Groups II and III with Group I) nor the use of pamaquin (Plasmo-chin) in the indicated dosage (compare Group II

with Group III) had any significant effect on the ultimate rate of relapse.

In Table 3 it is seen that of all the relapses that occurred up to six or seven months after completion of treatment with quinacrine, 60 per cent took place within sixty days and 90 per cent within four months. The higher percentage of relapses in

TABLE 2 Number of Relapses following Treatment with Quinacrine \*

	GROUP I	GROUP II	GROUP III	TOTALS
Number of patients	124	86	77	287
Number of relapses†	92	52	49‡	193
Percentage of relapses	74	60	64	67

\*All patients received 0.2 gm of quinacrine every 6 hours for five doses, followed by 0.1 gm three times a day for 6 days, until a total of 2.8 gm. had been given. At the completion of this therapy, the patients in Group I received no further treatment; patients in Group II received no treatment for 1 day, followed by 0.01 gm of pamaquin three times daily for 3 days, followed by 0.1 gm of quinacrine daily except Sunday until 60 days had elapsed from the institution of treatment. The patients in Group III received the same prolonged treatment as did those in Group II except that pamaquin was omitted, starting immediately after completion of the initial treatment with quinacrine.

†All relapses noted were proved by the finding of a positive blood smear with the exception of 2 patients, they occurred within 180 days after completion of treatment (Table 3). The mean days of observation of the patients without relapses and the probable errors of the means were as follows: Group I, 143.2±7.4; Group II, 119.9±3.7; Group III, 126.0±4.6. The differences between the means were in all instances less than three times the probable errors of the differences.

‡Includes 4 patients who had relapses while receiving small doses of quinacrine (Table 4).

the first month after completion of suppressive treatment (compare Groups II and III with Group I) may be related to the fact that plasma quinacrine concentrations at the completion of treatment of

TABLE 3 Length of Time before Relapses \*

TIME INTERVAL BEFORE RELAPSE†	GROUP I (124 CASES)		GROUP II (86 CASES)		GROUP III (77 CASES)		TOTAL (287 CASES)	
	No.	Per-centage‡	No.	Per-centage‡	No.	Per-centage‡	No.	Per-centage‡
days								
Less than 30	6	7	5	10	11§	23	22§	11
30-59	45	55	23	54	25	74	93	60
60-89	21	78	15	83	8	90	44	82
90-119	12	91	5	92	2	94	19	92
120-149	3	95	2	96	1	96	6	95
150-179	3	100	1	98	1	98	7	99
180-209	—	—	1	100	1	100	2	100
Totals	92		52		49		193	

\*For explanation of treatment in Groups I, II and III, see footnote to Table 2.

†Calculated from time of completion of quinacrine treatment.

‡Cumulative.

§Includes 4 patients who had relapses while receiving prolonged treatment with small doses of quinacrine.

the patients in Group I averaged approximately 45 microgm per liter, as compared with 25 microgm in Groups II and III (Fig. 1).

Although the use of 0.1 gm of quinacrine daily for sixty days had no significant effect on the ultimate relapse rate, there were only 4 relapses among 163 patients while they were on such continued small doses (Table 4). This extremely low incidence supports the observation in overseas theaters that the supervised administration of this dosage is an effective means of suppressing clinical malaria.<sup>8</sup>

In the two groups of patients given continued small doses, plasma quinacrine concentrations were determined each day during the initial week of

fasting concentrations from the second through the eighth day were 42 to 51 microgm per liter, whereas the average postprandial values two to

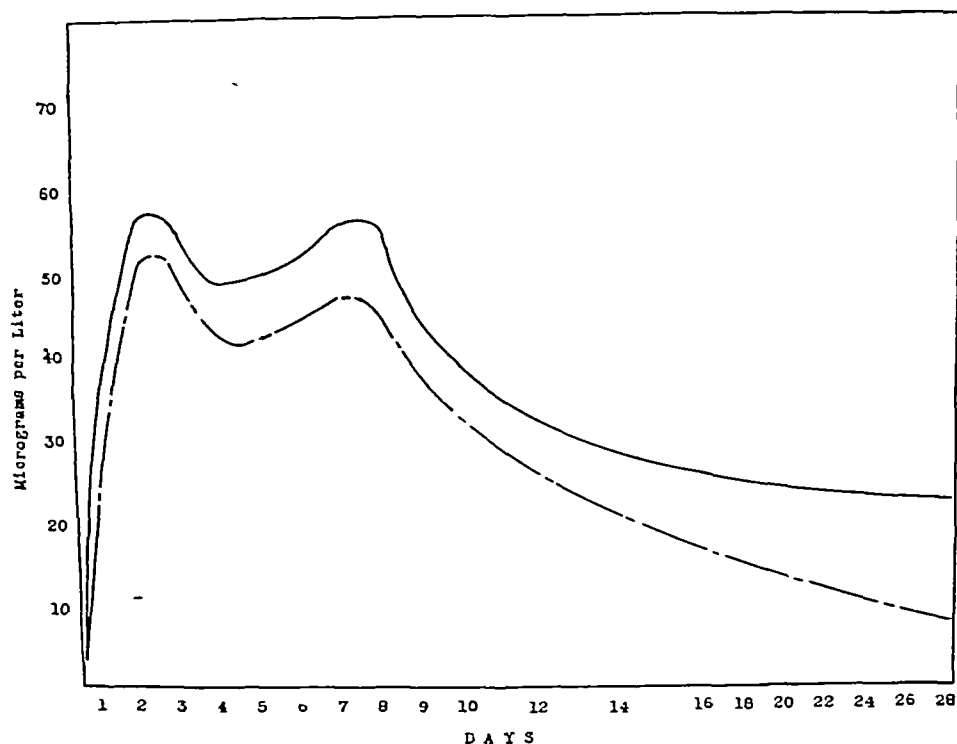


FIGURE 1 Comparison of Plasma Quinacrine Concentrations at Different Times

The broken line represents the average fasting plasma level in 104 patients given 2.8 gm of quinacrine in one week, the solid line that of 226 patients given the same amount of quinacrine in one week, followed by 0.1 gm of the drug on six days of each week. The latter specimens were taken 4 hours after administration of 0.1 gm of quinacrine.

treatment. As shown by Table 5, there was no relation between the plasma concentrations and the rate of relapse.

#### LABORATORY FINDINGS

**Plasma quinacrine concentrations.** The plasma concentrations<sup>9</sup> obtained with the oral administra-

four hours after breakfast — on the second through the seventh day quinacrine was given three times a day with meals — were somewhat higher, being

TABLE 4 Relapses during Treatment with 0.1-gm Daily Doses of Quinacrine (4 Cases)\*

CASE NO	INTERVAL AFTER COMPLETION OF QUINACRINE THERAPY, days	PLASMA QUINACRINE LEVEL ON DAY OF RELAPSE, microgm./l.	PRECIPITATING FACTORS
1	20	24	None known
2	35	35	Measles
3	5	30	Lobar pneumonia
4	37	15	Repeatedly low plasma concentrations during four relapses

\*These patients had smears and plasma quinacrine determinations every 5 days during the period of suppressive therapy. All of them had parasitemia a temperature of over 100°F and generalized aches, with the exception of one (Case 1) whose highest temperature reading was 99.2°F.

TABLE 5 Relation of Relapse to Average Plasma Concentration of Quinacrine\*

PLASMA QUINACRINE LEVEL†, microgm./l.	GROUP II†		GROUP III†	
	NO OF PATIENTS	PERCENTAGE OF RELAPSES	NO OF PATIENTS	PERCENTAGE OF RELAPSES
20-39	27	41	17	59
40-59	35	63	37	65
60-79	24	79	20	65
80 or higher	0	0	3	66
Totals	86		77	
Average percentages		60		64

\*No patient was counted who had not been observed either until a proved relapse had occurred or for 60 days following cessation of treatment.

†See footnote to Table 2 for outline of treatment in Groups II and III.

‡Average value during first week of treatment.

tion of 2.8 gm of quinacrine in one week were determined in 226 patients during attacks. The results (Fig 1) are comparable to those reported by Shannon and his co-workers<sup>10</sup>. The average

49 to 57 microgm per liter. With these concentrations the symptoms of the attack were usually abolished within seventy-two to ninety-six hours. No attempt was made to determine the minimum effective dose, which presumably varied with the density of the parasitemia and the patient's immunity. Following cessation of quinacrine therapy,

the plasma concentration slowly fell, so that by four weeks after the initial dose the average value was 8 microgm per liter. The latter level is below the effective suppressive treatment level of 20 to 25 microgm attained when 0.1 gm of quinacrine was administered six days a week.

**Complement-fixation reaction.** In the past, attempts to obtain a specific complement-fixation reaction with serums from human beings infected by *P. vivax* have led to inconclusive results. Since there are no certain clinical criteria indicative of a complete cure in vivax malaria, a complement-fixation test that could detect latent malaria would obviously serve an extremely useful purpose. The results of such a test with the use of an antigen prepared by Coggeshall and Frisch<sup>11</sup> from the chicken parasite *P. gallinaceum* are shown in Table 6. There

TABLE 6 Results of Complement-Fixation Tests during 234 Malarial Attacks and during Intervals Between 100 Observed Attacks

DAY OF ATTACK	NO OF TESTS	NO OF POSITIVE TESTS	NO OF ANTI-COMPLEMENTARY TESTS	PERCENTAGE OF NEGATIVE TESTS
1st	234	123	11	43
2nd	234	130	8	41
3rd	234	109	18	46
4th	234	127	10	41
5th	234	121	13	43
Interval tests	891	287	30	64

was a maximum of 58 per cent positive tests on any one of five successive days during 234 recurrent attacks. During intervals between 100 proved attacks, 64 per cent of 891 tests made at five-day intervals were wholly negative. Although the complement-fixation test gave a group reaction for the serums of human beings infected by *P. vivax*, it did not detect latent malaria as proved by subsequent relapses in a sufficiently high percentage of cases to be of practical value.

**Liver-function tests.** Liver function was investigated in patients with recurrent attacks of malaria (Table 7). During the attacks transient disturbances were noted, as indicated by the results with the icteric index, serum bilirubin concentration, urine urobilinogen, bromsulphalein-clearance and cephalin-flocculation tests. Following attacks, only 5 per cent or less of the patients showed evidence of impairment by the cephalin-flocculation (Wilson antigen), bromsulphalein and galactose-tolerance tests. With a more sensitive reagent (Difco antigen), 20 per cent of the cephalin-flocculation tests were abnormal, but since neither antigen is standardized, this divergence in sensitivity cannot be interpreted. With both antigens, however, the trend was toward normalcy after the acute attack had subsided. Neither multiple attacks of malaria nor treatment with quinacrine resulted in evidence of permanent hepatic dysfunction.

#### SUMMARY AND CONCLUSIONS

Clinical and laboratory findings are presented for 808 soldiers admitted to the Malaria Section

of the Harmon General Hospital from Pacific areas.

In 864 clinical attacks proved by positive smears, *Plasmodium falciparum* was demonstrated in only 1, and then as part of a mixed infection with *P. vivax*.

The administration of adequate doses of quinacrine caused prompt disappearance of parasites from the blood stream. Without lessening the

TABLE 7 Incidence of Abnormal Tests of Liver Function during and following Attacks of Malaria

TYPE OF TEST*	No IN GROUP		PERCENTAGE OF ABNORMAL TESTS						
	DURING ATTACK	AFTER ATTACK	DURING ATTACK					AFTER ATTACK	
			Day of Illness						
			1	2	3	4	5		
Serum icteric index	108	260	16	12	2	1	1	3	
Serum bilirubin	108	260	20	15	4	1	1	4	
Urine urobilinogen	176	227	20	19	14	4	3	1	
Bromsulphalein retention	151	149	4				1	3	
Cephalin flocculation (Difco antigen)	42	204	71	86	88	81	86	20	
Cephalin flocculation (Wilson antigen)	42	204	10	29	21	17	29	5	
Galactose tolerance		207						3	
Serum protein		172						2	
Serum cholesterol		156						0	
Serum phosphatase		191						0	

\*The following standards were used as an index of abnormality: icteric index, more than 8 units per 100 cc serum bilirubin, more than 0.5 mg. per 100 cc, urine urobilinogen, positive in a dilution higher than 1:20; bromsulphalein retention of more than 4 per cent in a specimen of blood taken 45 minutes after injection of 5 mg. per kilogram cephalin flocculation, positive flocculation; galactose tolerance, excretion of more than 3 gm. in 5 hours after ingestion of 40 gm. of galactose; serum protein, less than 6.0 gm. per 100 cc; serum cholesterol, more or less than 150-250 mg. per 100 cc; serum phosphatase, more than 5 Bodansky units per 100 cc.

need for good mosquito control, this indicates that early diagnosis and treatment of relapses will help to prevent the spread of the infection in this country.

Symptoms of the acute attack were rapidly controlled by the administration of quinacrine in doses that yielded a fasting plasma concentration of 40 to 50 microgm per liter.

Following such treatment, 67 per cent of 287 patients had proved relapses in a period of six or seven months. Approximately 50 per cent of these relapses occurred within sixty days after completion of treatment. There was no relation between the plasma quinacrine levels obtained and the rate of relapse.

The complement-fixation test with an antigen prepared from *P. gallinaceum* gave a positive reaction in approximately 50 per cent of tests performed on each of the first five days of 234 recurrences, but 64 per cent of 891 tests performed during the intervals between 100 proved attacks were wholly negative. In its present form the test does not detect latent malaria, as proved by subsequent relapses, in a sufficiently high percentage of cases to be of practical value.

Multiple tests of liver function during and following attacks showed no evidence of permanent hepatic dysfunction.

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## LONGEVITY WITH VENTRICULAR ANEURYSM

### Report of a Case with a Survival Period of Fifteen Years

CAPTAIN SIDNEY L. PENNER, M.C., A.U.S., AND CAPTAIN MICHAEL PETERS, M.C., A.U.S.

THE duration of life after an acute coronary-artery occlusion has long been regarded as brief, and it is only in recent years that the more optimistic viewpoint pronounced in 1912 by Herrick<sup>1</sup> has been justified. In increasing numbers, cases have been reported of survivals for as long as seventeen, twenty-four and even forty years<sup>2-5</sup>

not so much because of the presence of the out-pouching of the ventricular wall per se, as because this phenomenon is indicative of extensive myocardial damage. Cases have been reported, however, in which the patients have survived for as long as eight to ten years<sup>9, 10</sup>. We present a case in which the patient survived a severe attack of

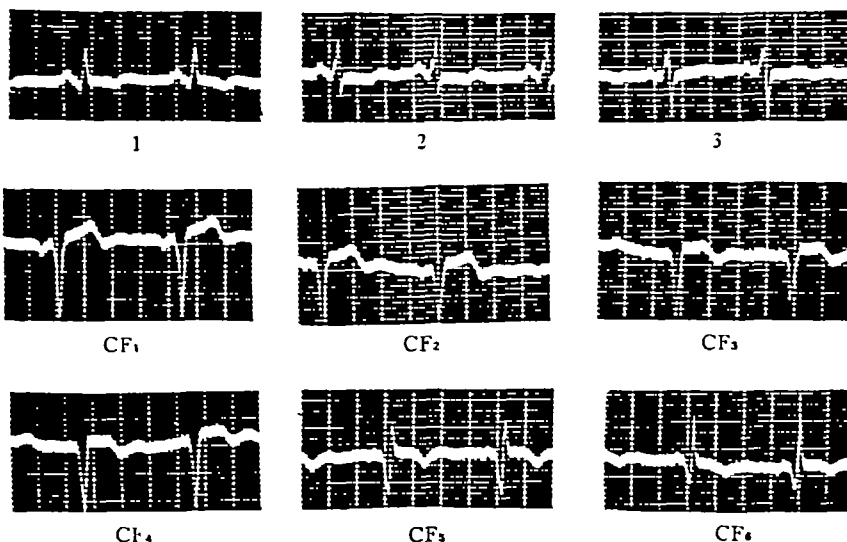


FIGURE 1

As an explanation of this change in prognosis, it has been suggested<sup>5</sup> that the myocardial infarction that is being diagnosed in mild and atypical forms would have been dismissed years ago as so-called "acute indigestion" or never have been brought to the attention of a physician, and that these forms have a more favorable prognosis than do the severer ones.

The prognosis of cases of ventricular aneurysm has heretofore been considered as particularly grave,<sup>6-8</sup> and the diagnosis has long been regarded as one to be made only at autopsy.<sup>7</sup> This is true

myocardial infarction with subsequent ventricular aneurysm and was alive and in reasonably good health fifteen years after the acute episode.

#### CASE REPORT

A 43-year-old infantry officer on October 25, 1929, had an episode of severe pain in the precordium and left arm while crossing a parade ground. He was unable to walk farther because of the pain, which gradually subsided when he stood still. He had no further symptoms until November 18, when while reading he was seized with agonizing chest pain, radiating to the left arm. He was extremely weak and restless but was not dyspneic. The examining physician found the patient in a state of shock, with mild cyanosis, profuse sweating, a cold clammy skin and a barely perceptible pulse.

Severe pain persisted for several hours despite the administration of 75 mg of morphine. During the following several days the temperature was elevated, reaching a maximum of 102°F. A loud pericardial friction rub was heard, and rales were audible at the base of the left lung. The blood pressure was 120/76. On December 3, the patient was seen in consultation by Dr. George H. Anderson, of Spokane, Washington. Inverted T waves were noted in the electrocardiogram. No further details of this examination are available.

For the first 6 weeks after the onset of the illness, the patient remained in bed at home and his general condition

ST interval in Lead 1. On March 30, there was another attack of severe cardiac pain, followed by slight fever for 4 or 5 days. The patient gradually improved from this time on but remained in the hospital until February, 1931, when he was retired from the Army.

For the next 2 years he had slight pain in the right chest and left shoulder and arm but no other symptoms. After 1934 he felt well and was active in building and sailing boats and doing deep-sea fishing. In September, 1942, because of the war, he was returned to limited duty and was able to work in an administrative capacity without symptoms until

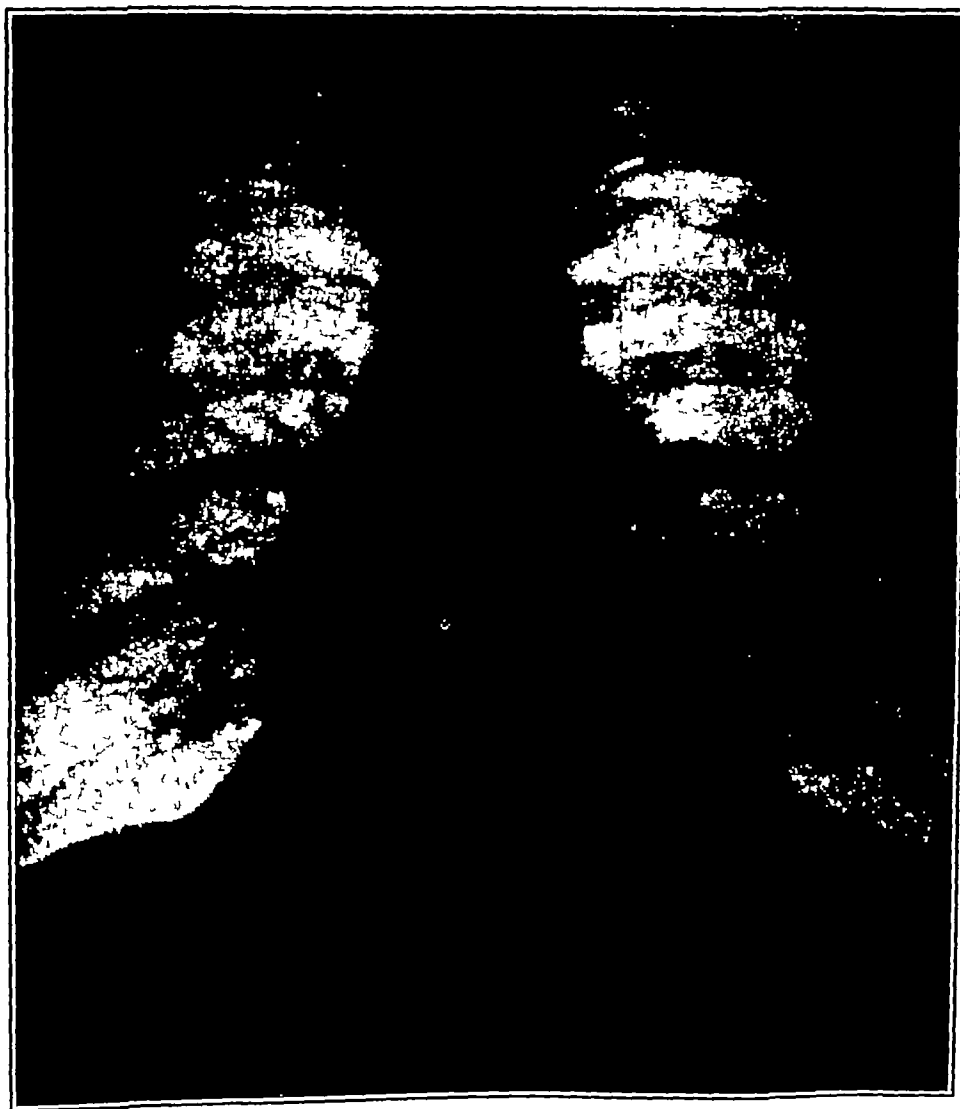


FIGURE 2

steadily improved. On January 31, 1930, he had a recurrence of pain, less severe than before but again followed by an audible pericardial friction rub. In February, he was transferred to a general hospital, where examination showed a traumatic cataract of the right eye and moderate thickening of the radial and brachial arteries. The blood pressure was 128/84. The heart was not enlarged, but the sounds were of poor quality and a soft systolic murmur was heard at the apex. There were no signs of congestive failure. The electrocardiogram showed a typical coronary T wave and

September, 1944. At that time he began to complain of pain in the left shoulder, radiating down the left arm and hand. There was occasional substernal distress, the pain being present at rest as well as on exertion. Cramps developed in the calves on walking and also on occasion during sleep. There was mild dyspnea on effort. An electrocardiogram was similar to those subsequently taken in April, 1945 (Fig. 1). Examination in that month showed thickening of the peripheral arteries. The blood pressure was 140/90. The heart was enlarged to the left on percussion, but there were no

thrills or abnormal pulsations over the precordium." The heart sounds were of good quality, and no murmurs were present. The first sound at the apex was split. No signs of congestive failure were present.

Electrocardiograms showed a regular sinus rhythm, left-axis deviation, slight slurring of the QRS complex in the limb leads, an inverted T wave in Leads I, CF<sub>1</sub>, CF<sub>2</sub>, CF<sub>3</sub> and CF<sub>4</sub>, elevation of the ST segment in Lead I and depression

knob. The roentgenologic interpretation was left-ventricular aneurysm with calcification of the outer ventricular wall and apparent cardiac enlargement because of rotatory displacement of the heart, due to ventricular aneurysm.

The laboratory findings, including a complete blood-cell count, urinalysis, determination of the blood sugar and urea and Kahn and sedimentation-rate tests, were normal. The patient was kept in the hospital for several weeks for study,



FIGURE 3

of ST segments in Leads 2 and 3. The QRS complex in Leads CF<sub>1</sub>, CF<sub>2</sub>, CF<sub>3</sub> and CF<sub>4</sub> was completely inverted, and a large Q wave was present in Leads CF<sub>1</sub> and CF<sub>2</sub>. X-ray examination of the heart showed the cardiac silhouette to be slightly enlarged (Fig 2). Overlying the left ventricular portion of the cardiac silhouette was seen a curvilinear, thin band of calcification forming the outer half of a soft-tissue condensation. Left lateral films showed encroachment of the left atrium on the esophagus. Fluoroscopic examination indicated that the calcification was in the outer surface of an outpouching of the anterior surface of the left ventricle. No pulsation was noted in this area. Bucky films taken in the right anterior oblique position (Fig 3) confirmed these findings and also showed calcification in the wall of the aortic

and on September 6, 1945, he was feeling well and again enjoying deep-sea fishing.

#### DISCUSSION

The diagnosis of cardiac aneurysm was not suggested by the physical findings,<sup>11, 12</sup> nor did the electrocardiographic findings fall into the pattern said to characterize this lesion,<sup>13</sup> although it was characteristic of extensive anterior myocardial infarction. The x-ray examination, however, made the diagnosis clear. The following roentgenographic

criteria have been suggested<sup>8</sup> for the diagnosis of ventricular aneurysm enlargement of the left ventricle with deformity of the cardiac contour, a localized protuberance of the silhouette, absent or abnormal pulsations under the fluoroscope, evidence of adhesions to the chest wall and calcification of the aneurysmal wall or intraventricular clot. Of these criteria, the present case showed the first, second, third and fifth. In addition, there was dorsal displacement of the esophagus.<sup>14, 15</sup>

Although the diagnosis of aneurysm was not established until 1945, it is justifiable to assume that the aneurysm was a direct result of the infarction or infarctions of 1929 and 1930. Ventricular aneurysm has been found to develop during the acute stage.<sup>16</sup> The severity of the recurrent seizures, with pericarditis and fever as manifestations, and the persistence of symptoms requiring hospitalization for more than one year testify to the extent of the myomalacia. The present aneurysm had probably existed for the entire fifteen-year period and may have increased in size with the passage of time. The calcification must have been many years in development. The recurrence of symptoms in 1944 may have been due to one or more minor episodes of infarction, but the aneurysm was obviously of much earlier origin.

Since ventricular aneurysm has been found to develop even during the acute stages of myocardial infarction,<sup>16</sup> and since the time for healing of an infarcted area has occasionally been found to be prolonged,<sup>17</sup> the precaution of confining the patient to the hospital for over a year seems justified. During the next fourteen years, the patient reaped the benefit of his long convalescence, being able to lead an active and almost symptom-free existence. In this period of hospitalization, during which the demands on the myocardium were kept at a minimum, the formation of new anastomoses between the right and left coronary arteries and dilatation of the pre-existing anastomoses could take place.<sup>18</sup> The enlargement of the defect in the ventricular wall under the impact of systole was diminished,<sup>19</sup>

and the danger of ventricular rupture was minimized.<sup>20, 21</sup> Had a less conservative approach<sup>22-24</sup> been employed, the result might have been disastrous.

### SUMMARY

A case of ventricular aneurysm with a survival period of fifteen years is reported and is discussed in relation to the therapeutic implications.

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OSSEOUS GAUCHER'S DISEASE WITH MACROCYTIC NORMOCHROMIC ANEMIA

Report of a Case

LIEUTENANT COLONEL ROBERT FIENBERG, M C , A U S , AND MAJOR GEORGE E. QUIGLEY, M C , A U S

IN THE typical cases of Gaucher's disease, the disturbance of the cellular metabolism, characterized by the accumulation and retention of the cerebroside kersin in the reticular and histiocytic cells, leads to the enlargement of the spleen and liver, with occasional osseous defects. In addition, there are pigmentation of the skin, pingueculae, leukopenia, microcytic, hypochromic anemia and hemorrhagic tendencies due to thrombocytopenia. In the case reported below, the most prominent manifestations of the typical case of Gaucher's disease were absent. In fact, the presenting finding was an anemia that was discovered by the patient himself while he was practicing routine red-cell counts using his own blood. Subsequent examination disclosed the unusual combination of a macrocytic normochromic anemia with Gaucher's disease in which the spleen and liver were not palpable. The diagnosis was made possible only by the examination of the long bone marrow, since the radiologic appearance of the bones was normal.

CASE REPORT

A 20-year-old, Jewish laboratory technician was inducted into the Army in April, 1943. In the following summer, while undergoing basic training, he suffered pain in the right hip. This subsided in 4 days without treatment. Early in May,

unt of the skin. The abdomen was soft. Tenderness was present in the right upper quadrant. The spleen was not palpable, and the edge of the liver, which was tender, could be felt only on deep inspiration. During his hospital stay, the patient complained of "gas on the stomach" and appeared sluggish and weak. The possibility of an attack of infectious hepatitis was entertained on account of the symptoms, the yellow tint in the scleras and skin, the tender liver and the increased blood bilirubin. Pain was still felt in the right hip. The feces were always formed and brown. The patient was treated with a high-carbohydrate, high-vitamin diet and bed rest. On August 21, he was returned to duty. It was planned to perform a sternal puncture in a month to elucidate the nature of the anemia.

On September 28, a sternal puncture was done and a diagnosis of Gaucher's disease of the osseous type was made. On October 8, the patient was readmitted for further study. He had been feeling sluggish and weak and had had a poor appetite. Pain had continued in the right hip and lower back. No other member of the patient's family suffered from Gaucher's disease, although an aunt died of an anemia the exact nature of which was unknown to the patient.

On physical examination, the spleen and liver were not palpable. The malar flush and the generalized slight yellow tint of the skin were still present. The yellowish tint in the scleras was discovered to be caused by definite bilateral pingueculae extending from the medial limbi of the corneae to the internal canthi. Roentgenograms of the entire skeleton revealed no lesions in the bones. On October 11, biopsies of the sternum and the left tibia were done. The sternal marrow did not look remarkable, but the tibia appeared devoid of marrow and a large amount of fluid blood came from the marrow cavity.

Pertinent data concerning the red cells and the hematologic indices and corpuscular constants are given in Table 1. On May 27, the white-cell count was 4850, with 45 per cent seg-

TABLE 1 Summary of Pertinent Laboratory Data

DATE	HEMOGLOBIN (SAHLI)	RED-CELL COUNT	HEMATOCRIT	RETICULOCYTES	VOLUME INDEX*	COLOR INDEX*	MEAN CORPUSCULAR VOLUME	MEAN CORPUSCULAR HEMOGLOBIN	MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION
	gm /100 cc	x10 <sup>6</sup>	%	%			cu. microns	micromicrogm	%
5/27	—	4.1	—	0.9	—	—	—	—	—
7/15	12.5	4.0	—	—	—	—	—	—	—
8/17	13.0	3.6	40	—	1.27	1.26	112	36.4	32.5
9/5	13.0	3.7	43	0.9	1.35	1.25	117.8	35.6	30.2
9/25	13.4	3.7	40	0.6	1.25	1.26	103.9	36.5	33.5
10/8	13.5	3.3	44	1.0	1.53	1.41	133.3	40.9	30.6
Normal					1.00	1.00	82-92	27-31	32-36

\*The figure of 43.2 per cent was taken as the normal mean volume of packed red cells, and 14.5 gm per 100 cc. as the normal hemoglobin.

1944, while the patient was playing baseball, another attack of pain developed in the right hip and lower part of the back, although there had been no trauma or extreme physical exertion. The patient was then practicing red-cell counts, using his own blood, and discovered that he had an anemia. Following this finding, a diagnosis of macrocytic anemia was made. Free hydrochloric acid was found in the stomach. In the meantime, the pain in the back, which had persisted, suggested the presence of a ruptured intervertebral disk, but examination of the cerebrospinal fluid on June 2 disclosed nothing of significance, and a neurologic examination was negative. The patient was given 15 mg of thiamine daily, and the hip and back pain subsided. On August 1, the patient reported to sick call complaining of epigastric distress, nausea and anorexia. Physical examination revealed a well developed and well nourished man not acutely ill. There was a slight yellowish tint in the scleras, as well as a malar flush and a generalized slight yellowish

mented neutrophils, 6 per cent band neutrophils, 43 per cent lymphocytes, 4 per cent monocytes and 2 per cent eosinophils. Slight anisocytosis and slight poikilocytosis were present. On August 17, the white-cell count was 7000, with 40 per cent segmented neutrophils, 4 per cent band neutrophils, 46 per cent lymphocytes, 7 per cent monocytes and 3 per cent eosinophils. On September 5, the white-cell count was 6900, with 46 per cent segmented neutrophils, 2 per cent band neutrophils, 38 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. Slight anisocytosis and slight poikilocytosis were present. On September 25 it was 8600, with 42 per cent segmented neutrophils, 15 per cent band neutrophils, 35 per cent lymphocytes, 3 per cent monocytes, 1 per cent eosinophils and 4 per cent basophils. Slight poikilocytosis was noted. On October 8, it was 5500, with 42 per cent segmented neutrophils, 12 per cent band neutrophils, 41 per cent lymphocytes, 3 per cent monocytes and 1 per cent eosinophils. Polychromatophilia, achromasia,

anisocytosis and poikilocytosis were present. No spherocytes were ever found. The platelet count was 250,000.

A red-cell fragility test on August 5 revealed that hemolysis began at 0.46 per cent saline solution for the patient and 0.46 per cent for the control and was complete at 0.36 per cent for the patient and 0.38 per cent for the control. Another test on October 8 showed that hemolysis began at 0.44 per cent for the patient and 0.46 per cent for the control and was complete at 0.36 per cent for the patient and 0.38 per cent for the control. The sedimentation rate (Westergren) was 11 mm per hour on August 6 and 24 mm on August 19, 1944. Two urinalyses were negative. Three Wallace-Diamond tests for urine urobilinogen disclosed no increase over the normal.

On May 26, 1944, a gastric analysis revealed 12 to 94 units of free hydrochloric acid and 28 to 106 units of total acidity. On May 28, no excess fat was found in the feces. On August 8, the blood nonprotein nitrogen was 33.9 mg per 100 cc and the blood cholesterol 200 mg.

The icteric indices and the corresponding quantitative bilirubin determinations (Van den Bergh reactions) are listed in Table 2. The Van den Bergh reaction was always indirect.

On August 7, the total serum protein was 8.2 gm per 100 cc and the albumin-globulin ratio 2:1. On August 8, the total serum protein was 7.2 gm and the albumin-globulin ratio again 2:1. In the Quick hippuric acid liver-function

blasts predominating. An occasional mitotic figure was found among the marrow cells. With the Giemsa stain, the Gaucher cells were pale, the cytoplasm being devoid of color. Otherwise the picture was similar to that found in the sections stained with hematoxylin and eosin. The Gaucher cells in sections stained with Mallory's aniline blue-orange G method were extremely prominent because their cytoplasm was stained blue. The cytoplasmic striations appeared to be accentuated, giving the cytoplasm a wrinkled appearance, and occasionally large vacuoles appeared in it.

The sternal marrow obtained by biopsy on October 11 was treated in the same way as was the sternal-puncture material. A direct smear stained with Wright's stain contained 8 per cent segmented neutrophils, 22 per cent band neutrophils, 8 per cent juvenile neutrophils, 13 per cent neutrophilic myelocytes, 4 per cent myeloblasts, 4 per cent pronormoblasts, 14 per cent normoblasts, 13 per cent lympho-

TABLE 2 Icteric Indices and Blood Bilirubin Levels

DATE	ICTERIC INDEX	BLOOD BILIRUBIN mg/100 cc
5/9	15.5	—
6/11	10.0	—
8/1	10.0	2.60
8/4	10.0	2.30
8/12	9.0	2.60
8/19	9.0	1.90
8/28	7.0	0.25
9/5	12.0	2.30
9/25	11.0	1.50

test (oral), the total excretion of hippuric acid amounted to 5.5 gm. On June 2, there were no white cells in the spinal fluid and the total protein was 32.3 mg per 100 cc.

The sternal-puncture material obtained on September 28 was smeared, and the small amount of blood clot remaining, which amounted to 0.4 cc., was placed in Zenker's fluid for sectioning. Staining of the direct smear with Wright's stain revealed 5 per cent segmented neutrophils, 32 per cent band neutrophils, 14 per cent juvenile neutrophils, 12 per cent neutrophilic myelocytes, 2 per cent myeloblasts, 2 per cent pronormoblasts, 11 per cent normoblasts, 18 per cent lymphocytes, 2 per cent monocytes, 1 per cent eosinophils and 1 per cent mitotic figures. In a general survey of the bone-marrow smears, scattered large cells were found, especially at the edges. These cells possessed abundant cytoplasm staining a light blue. Within the cytoplasm there were scattered striations, giving it a reticulated appearance. Infrequently a small vacuole was seen, and more rarely a purplish dot was found near the nucleus. The nuclei varied in shape, some being round and others slightly indented. In addition, multilobated and multinucleated types were noted. The chromatin pattern formed a coarse, open meshwork. The small blood clot fixed in Zenker's fluid was handled by the usual method for tissues. Examination of paraffin sections stained with hematoxylin and eosin revealed the presence of small fragments of marrow within the blood clot. Much of the marrow had been extensively replaced by compact masses of Gaucher cells. These large cells possessed abundant delicately striated cytoplasm. Many of the striations were arranged in concentric lines about the nucleus. Frequently the cytoplasm was diffusely yellowish brown. Ingestion of red cells by occasional Gaucher cells was noted, especially by those the cytoplasm of which was pigmented. Infrequently, acicular spaces were noted in the cytoplasm. Many of the nuclei were multiple or multilobated, whereas others were round or indented. Most of the nuclei were vesicular, with occasional large nucleoli. No mitotic figures were seen among these large cells. Among the marrow cells still remaining there was active hematopoiesis, with normo-

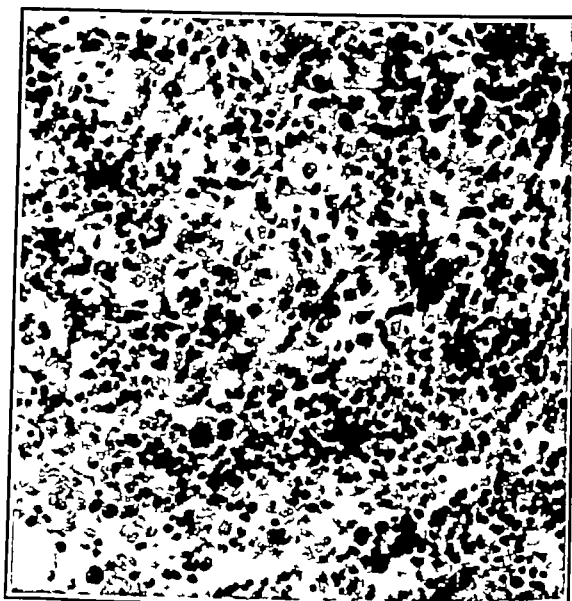


FIGURE 1 Group of Gaucher Cells Infiltrating the Sternal Marrow (x 225)

cytes, 10 per cent Gaucher cells, 3 per cent monocytes and 1 per cent mitotic figures. Megakaryocytes and platelets were few. The appearance of the cells was similar to that in the direct smear of the sternal puncture. The marrow in the blood clot obtained by the first sternal puncture, except that the material was more abundant. In addition, the fatty tissue in the marrow was scanty and some of the Gaucher cells assumed a spindle appearance. The bone trabeculae were not remarkable. The Gömöri stain for hemosiderin stained the yellowish-brown pigment in the cytoplasm of the large cells blue, and the pigment was thus identified as hemosiderin. Sudan IV, the Schultz stain for cholesterol and the Smith-Dietrich stain were applied to direct smears of the sternal marrow, but none disclosed the presence of lipoids. The biopsy of the tibial marrow yielded little material. The direct smear consisted mainly of red cells, with a rare Gaucher cell. In paraffin sections, a small fragment of marrow was found in a blood clot that possessed the characteristics of the sternal marrow. A diagnosis of Gaucher's disease was made after microscopic examination of both the sternal and tibial marrows. Biopsy examination of the skin of the right flank on October 23 revealed no pigmentation or other abnormal details.

#### DISCUSSION

Several characteristics of this case deserve comment. Outstanding is the macrocytic, normo-

chromic anemia, a normochromic anemia being defined as one with a mean corpuscular hemoglobin concentration of 30 per cent or more. The lack of a palpable spleen and liver and of roentgenologic changes in the skeleton and the presence of bone pain and latent jaundice also merit attention.

According to Thannhauser,<sup>1</sup> the anemia in Gaucher's disease is usually microcytic, although he admits that the anemia may become macrocytic in the terminal stages of the disease. Pick<sup>2</sup> and Capper, Epstein and Schless<sup>3</sup> state that the anemia is usually hypochromic, whereas Wintrobe<sup>4</sup> describes it as normocytic and Mandlebaum and Downey<sup>5</sup> call it chlorotic. Bloem, Groen and Postma<sup>6</sup> reported 4 cases. In 1 the mean corpuscular volume was 108 cubic microns with a color index of 1.2, but the other 3 showed a hypochromic anemia. In the case reported by Melamed and Chester,<sup>7</sup> there was a marked hypochromic microcytic anemia, but one examination out of twenty-one showed a macrocytosis. Finally, there was a hypochromic anemia in Petit and Schleicher's<sup>8</sup> case. It is thus evident that the finding of a macrocytic normochromic anemia is unusual, but in the light of Davidson and Fullerton's<sup>9</sup> report on the rare types of macrocytic anemia it is not unexpected, since infiltration of the marrow by the neoplastic cells found in some of their cases closely resembles the mechanism present in osseous Gaucher's disease, although the Gaucher cells are not per se neoplastic.

Most other writers are agreed that enlargement of the liver is usually an accompaniment of an enlarged spleen. As for the spleen, Thannhauser<sup>1</sup> states that it is always enlarged, and Krumbhaar<sup>10</sup> emphasizes the importance of the size of the spleen in making a diagnosis of Gaucher's disease. Pick,<sup>2</sup> on the other hand, after studying cases of bone involvement by Gaucher cells in which the weight of the spleen and liver was less than the average weight of these organs in Gaucher's disease, directed attention to an osseous form that he considers to belong to a subgroup having a special constitutional predisposition for the skeletal system, so that occasionally all members in a family afflicted with the disease have a predominant involvement of the bones. Thannhauser<sup>1</sup> prefers not to set up a separate category but holds that the involvement of the skeleton is as constant as is involvement of the spleen. The latter is likely, but why the spleen should remain small in cases of Gaucher's disease in which the skeleton is involved, as in our case, is puzzling, nor is the solution of the puzzle advanced by the disclosure of the presence of Gaucher cells postmortem in a spleen weighing 100 gm. in the case of Petit and Schleicher,<sup>8</sup> in which there was also marked bone involvement. In the present case, the explanation may lie in the early stage of the disease, but this seems less probable in the case of Petit and Schleicher,<sup>8</sup> in which the patient was seventy-nine years old.

It must be emphasized that the bones may be infiltrated by Gaucher cells without visible changes in the roentgenograms. This phenomenon is evident in our case and in that of Petit and Schleicher,<sup>8</sup> and in both, diagnosis was made possible only by the examination of the sternal marrow. The diagnosis of Gaucher's disease in a man of fifty-two reported by Vogel, Erf and Rosenthal,<sup>11</sup> in whom no enlargement of the spleen or liver could be found, was also made by sternal puncture. In this case rarefaction of the bones could be seen in the roentgenogram.

In many cases of osseous Gaucher's disease, the presence of bone pain has led to erroneous diagnoses. Thannhauser<sup>1</sup> points out that bone pain, accompanied by fever, may be an early symptom and may simulate rheumatic pain. On the other hand, acute osteomyelitis may be mistakenly diagnosed, as happened in the case of Capper, Epstein and Schless.<sup>3</sup> Welt, Rosenthal and Oppenheimer<sup>12</sup> also emphasize the presence of bone pain in this disease. In the present case, the diagnosis of a ruptured intervertebral disk was considered on account of the low-back pain, but a negative neurologic examination and normal findings in the cerebrospinal fluid aided in discarding this possibility.

The occurrence of jaundice is considered by Krumbhaar<sup>10</sup> to be rare, whereas Thannhauser<sup>1</sup> states that a slight transient jaundice is an exception. According to Mandlebaum and Downey,<sup>5</sup> it is absent. The last authors refer to jaundice that is clinically perceptible. A perusal of the reports in the literature, however, discloses the presence of latent jaundice in some cases of Gaucher's disease, including the osseous types. In fact, it was present in one of Thannhauser's<sup>1</sup> cases, and the statement that there may be a positive indirect van den Bergh reaction in cases of Gaucher's disease may be found in his review. In addition, latent jaundice was found in the case of Petit and Schleicher.<sup>8</sup>

The explanation of the mechanism of the production of latent jaundice in the osseous cases without enlargement of the liver has not been found in the literature and is open to speculation, especially since in the autopsied case of Petit and Schleicher<sup>8</sup> no Gaucher cells were found in the liver, which appeared little altered from the normal. In the latter case, a hemolytic process may have been active, although no evidence was presented to support this. A definite hemolytic process was present, however, in a case of Gaucher's disease reported by Mandlebaum, Berger and Lederer,<sup>13</sup> in which a diagnosis of hemolytic anemia was made. The possibility exists that a hemolytic process was active in our case also, but unfortunately no elevated urinary urobilinogen excretion was revealed by the Wallace-Diamond test, nor could reticulocytosis be detected. On the other hand, the presence of abundant hemosiderin in the Gaucher cells and the active erythrophagia by the same cells in the marrow in the present case

suggest that destruction of red cells was proceeding, but at such a slow rate that reticulocytosis and increased urinary urobilinogen did not appear. It was impossible to determine the amount of fecal urobilinogen excreted.

The deposition of hemosiderin in Gaucher's disease has been emphasized by Pick,<sup>2</sup> who believes that there is a storage of hemoglobinogenic pigments in lipid-storing cells. In fact, he states that hemosiderosis — or rather, increased blood destruction — occurs when the reticuloendothelial system is stimulated. This theory is probably too general, since hemosiderosis does not occur in Niemann-Pick's disease,<sup>2</sup> although here other factors, such as the age of the patient and the rapidity of the course of the disease, may contribute to the absence of the hemosiderin. It is well established that hemosiderin is either absent or extremely scarce in children with Gaucher's disease.<sup>2</sup> It is thus possible that erythrophagia and hemosiderosis vary in intensity in cases of Gaucher's disease and that it is in those in which the hemolytic process is at least moderately active that latent jaundice or even frank jaundice occurs.

That the episode of epigastric distress, nausea and anorexia in the case reported herein was due to an attack of infectious hepatitis is doubtful. Certainly at that time there was no rise in the blood bilirubin over that usually found in this patient, and there was no increase in the size of the liver.

It is true that the presence of the Gaucher cells in the marrow, with their characteristic wrinkled cytoplasm staining blue with Mallory's aniline blue-orange G stain and containing hemosiderin but no stainable lipid, made possible an unequivocal diagnosis, but before an examination of the marrow could be carried out other diseases in which a macrocytic normochromic anemia and an elevated blood bilirubin occur had to be ruled out.

Some of the diagnostic possibilities were pernicious anemia, nutritional macrocytic anemia, achrestic anemia, cirrhosis, congenital and acquired hemolytic jaundice and familial nonhemolytic jaundice. Sickle-cell anemia may be macrocytic and is accompanied by a hyperbilirubinemia, but this was not seriously considered on account of the race of the patient. Most of these possibilities were discarded through the data obtained from the clinical history, the physical examination and the laboratory studies other than that of the sternal marrow. Of all the suggested conditions, achrestic anemia and

familial nonhemolytic jaundice remained after the above studies were carried out. These were quickly discarded after an examination of the sternal marrow. Certainly, the demonstration of Gaucher's cells in the sternal marrow in this case offers another example of the value of sternal biopsy or puncture in the elucidation of blood dyscrasias.

#### SUMMARY

The diagnosis of a reported case of Gaucher's disease was made difficult by the presence of a macrocytic normochromic anemia with latent jaundice and by the lack of an enlarged spleen and liver, together with the lack of roentgenologic changes in the bones.

The sternal puncture alone made possible the diagnosis by the demonstration of Gaucher cells in the marrow. Once again, the value of sternal puncture in differentiating the blood dyscrasias has been proved.

It is suggested that the probable mechanism responsible for the production of the latent jaundice rested on the active erythrophagia of the Gaucher cells.

We are indebted to Dr. L. C. D. Hermitte, pathologist of the Sheffield Royal Infirmary, for the suggestions concerning the pathogenesis of the latent jaundice and for the photomicrograph.

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## MEDICAL PROGRESS

### SURGERY OF THE HEART AND STRUCTURES RELATED TO IT (Concluded)

JOHN W. STRIEDER, M.D.\*

BOSTON

#### TRAUMA

##### Wounds

What can be accomplished in the reduction of the mortality from wounds of the heart is ably demonstrated in a paper by Elkin<sup>12</sup> from the Department of Surgery at Emory University. Abstracts of the histories of 23 patients operated on for wounds of the heart are presented. In this series, the mortality rate was 22 per cent, as compared with 42 per cent in 38 cases previously reported from the same department. Although it has generally been considered that the intravenous administration of fluids prior to operation in cases of acute pericardial tamponade is contraindicated because of the danger of increasing the hemorrhage and hence the degree of tamponade, Elkin believes that such infusions have a beneficial effect by increasing the blood volume and hence the cardiac output. This point of view is based on the experimental work of Cooper et al.,<sup>14</sup> who produced pericardial tamponade in dogs and then gave saline solution intravenously, with striking improvement.

Immediate operation was undertaken in all Elkin's cases, being performed as soon as the diagnosis had been made. As evidenced by the reported cases from other clinics, however, aspiration of the pericardium, either as a temporary or a definitive measure for the treatment of cardiac tamponade, may be properly employed.

##### Foreign Bodies

During the course of a war characterized by a high caliber of the medical services, many noteworthy papers dealing with the surgery of trauma of the thorax have naturally appeared. The experiences of Harken and his associates,<sup>15-17</sup> in connection with foreign bodies in and close to the thoracic blood vessels and heart are particularly worthy of review, since they deal with practical aspects of intracardiac surgery, hitherto largely of theoretical conception as regards human beings.

These workers have removed missiles from within or adjacent to the great vessels of the thorax in 79 cases, in 3 of which the missiles were embolic. The latter were removed by Harken.<sup>18</sup> His search of the literature revealed nearly 40 cases of embolic foreign bodies, but there were no examples of successful removal of embolic missiles from the great intra-

thoracic blood vessels. Harken assumes, however, that when all the reports of thoracic surgery performed in World War II have been published, these will include additional cases of successful removal of embolic missiles from these vessels. In the first of Harken's cases with removal, adequate roentgenograms were taken before embolization, and the embolus apparently moved from the liver to the left pulmonary artery. In the second case, movement was apparently through the heart and the embolus lodged in the innominate artery. In the third case, the embolus moved at operation from the left to the right pulmonary artery and was successfully removed from the right side at a second operation.

Harken and his associates state that certain foreign bodies impinging on the great vessels of the chest are removed to prevent erosion and hemorrhage or infection. In 15 per cent of the cases in this series the missiles were in abscesses, in 30 per cent, they were associated with other foreign material, such as bone or clothing, and in 67 per cent, they grew pathogenic organisms on culture.

In 59 cases, foreign bodies were removed from within or in immediate relation to the heart. In 13 of these, they were taken from the chambers of the heart. The indications for the removal of foreign bodies in the heart were originally set up on the basis of the medical literature, Harken's experimental work on dogs before the war and certain theoretical grounds. They are as follows: to prevent embolus (a foreign body or thrombus), to reduce the danger of bacterial endocarditis, to prevent recurrent pericardial effusions, and to diminish the incidence of cardiac rupture or myocardial hernia. It was believed that all four of these indications were supported by their own clinical experience and that of their colleagues. In addition, pain and cardiac neurosis may constitute indications for intervention.

Harken emphasizes that he and his associates elected to leave behind more foreign bodies than they elected to remove. Size and clinical manifestations were inevitable factors influencing their decision to operate. Small foreign bodies were thought possibly to be associated with less damage and to be less likely to cause the above complications than larger ones. They were, moreover, technically more difficult to remove. Inasmuch as it cannot be definitely ascertained from the literature just how hazardous retained intracardiac

\*Visiting surgeon in charge of thoracic surgery, Massachusetts Memorial Hospitals and Boston City Hospital; assistant professor of thoracic surgery, Boston University School of Medicine.

foreign bodies are, and because some patients have undoubtedly remained asymptomatic for many years, the authors are reluctant to be dogmatic. They believe, however, that figures in the literature are misleading, because in many cases only roentgenograms were used in localizing the foreign body that was called intracardiac. They doubt whether some of these missiles were intracardiac, since in their own experience, in less than half the cases referred to them as having intracardiac foreign bodies, these were found on careful fluoroscopic examination to be in the heart. Furthermore, almost a third of the missiles that had been regarded as intracardiac were found at operation to be extracardiac. As these authors' experience widened, they felt justified in broadening their indications, since they had no deaths and since certain complications, some of them lethal, were observed to occur when the foreign bodies were left alone.

In the surgical procedure followed by Harken et al, the approach to the heart varies with the individual case and is planned so that minimal dislocation of the heart is necessary. The sternum, cartilage and ribs may be divided, but nothing is removed and no tissue is discarded. When adequate exposure is obtained, two rows of U sutures are placed on either side of the proposed cardiomy incision. These sutures are used as hemostatic sutures between manipulations and after the foreign body has been extracted with forceps. The myocardium is closed by approximating the margins of the incision with the inner row of hemostatic sutures and using the outer row to hold a pericardial graft in place.

In a dramatic case, three successive cardiomyotomies were performed at suitable intervals before the foreign body, which migrated twice, was successfully removed. It was originally in the right ventricle but moved to the right auricle at the first operation. When approached from the right side at the second operation, it moved from the right auricle back to the right ventricle. Because the patient was placed in the reverse Trendelenburg position with the right side elevated, the foreign body remained in the right ventricle during the third cardiomyotomy, when it was successfully removed. Reoperation in this case gave a valuable opportunity to note the manner of healing of the myocardial incision. The myocardial scar was firm and well healed six months after the original incision, a fact that to Harken offers assurance that the injury to the myocardium caused by the incision and exploration of the ventricle is not significant.

The cases previously referred to and subsequent ones represent 138 patients and one hundred and forty-three operations. There were no deaths.

#### ACUTE PERICARDITIS

*Streptococcus viridans* is rarely encountered as the causative agent in purulent pericarditis. Hargrove<sup>19</sup>

reports a case in a sixteen-year-old boy with acute pericarditis resulting from a *Str viridans* septicemia that followed an upper respiratory infection. The organism was twice found in cultures of blood and pericardial fluid. The author suggests that electrocardiograms be made during septicemia, pneumonia and osteomyelitis if there is a suspicion of pericardial disorder. In the case reported, pericardiocentesis and electrocardiography indicated acute pericarditis. The patient was treated by aspiration and sulfanilamide, but the disease ran a stormy course and the outcome was at first doubtful, although there was an eventual recovery.

Wise and Shafer<sup>20</sup> report a case of pericardial effusion secondary to lobar pneumonia in a woman of thirty-one. Sulfadiazine and intramuscular penicillin had no effect on the lesion, but there was dramatic response to the intrapericardial injection of penicillin following pericardiocentesis and the removal of 70 cc of turbid blood-tinged fluid. A dose of 40,000 units of penicillin in 30 cc of normal saline solution was introduced directly into the pericardial cavity. Within sixteen hours the temperature dropped to normal. Penicillin was continued in decreasing doses intramuscularly for four or five days.

The number of cases of suppurative pericarditis treated by the intrapericardial instillation of penicillin has not been sufficiently large to permit any valid conclusions concerning the efficacy of this treatment. Undoubtedly, certain patients are cured by this method alone, as is true in cases of empyema thoracis, particularly those with a nonputrid empyema. As has been reported by a number of observers,<sup>21, 22</sup> however, in the treatment of empyema with penicillin one may sterilize the fluid or pus by vigorous therapy, only to see a recurrence within two weeks. In other cases, the persistence of thick pus and fibrin clots, even though sterile, with consequent organization and thickened pleura, renders the expansion of the collapsed lung impossible or at least subject to long delay. It has therefore been recognized that persistent purulent accumulations in the pleura, even though sterile, should have surgical drainage. I have had the same experience in the treatment of empyemas complicating pulmonary resections, and Lynch and I have found this to be true in the treatment of putrid empyema.<sup>23</sup>

If the same situation obtains with regard to intrapericardial penicillin therapy, the patient should sooner or later present evidence of constrictive pericarditis. Patients who have had such therapy should therefore be carefully observed so that their status in this regard may be evaluated.

Urschel et al<sup>24</sup> discuss 8 cases of acute pericarditis that they observed during a period of three months. They devised a graph to correlate the heart size, total T-wave deflection, total elevation of the RS-T segment, pericardial friction rub and temperature. Judging from the cases observed, there is no sig-

nificant electrocardiographic difference in the pericarditis caused by rheumatic fever, tuberculosis or pneumococcal or meningococcal infection

Acute pericarditis simulating myocardial infarction is discussed by Wolff<sup>25</sup> He states that pericarditis unassociated with other diseases may be characterized by pain resembling that of acute myocardial infarction, and that great care must be used in differential diagnosis, since treatment and prognosis of the two conditions are markedly different. In the several cases of acute pericarditis described by the author, the correct diagnosis was established by the careful study of clinical, laboratory, electrocardiographic, teleroentgenographic and fluoroscopic data

### CONSTRICTIVE PERICARDITIS

The use of partial pericardiectomy and epicardiolysis in 24 cases of constrictive pericarditis is discussed by Harrington<sup>26</sup> The two most frequent conditions with which constrictive pericarditis is likeliest to be confused clinically are cirrhosis of the liver and congestive heart failure from intrinsic cardiac disease In most cases, however, the subjective symptoms of constrictive pericarditis are sufficiently characteristic so that when they are correlated with the physical and laboratory findings a definite diagnosis can be made

The laboratory findings are extremely valuable in establishing a diagnosis The venous pressure is elevated above normal The circulation time of the blood is increased The tests of hepatic function indicate a varying degree of hepatic damage, which depends to some extent on the duration of the disease. Roentgenologic studies of the heart in cases of constrictive pericarditis usually show it to be normal or smaller than normal It is never markedly enlarged or segmentally dilated, as in congestive heart failure from intrinsic cardiac disease and hypertensive heart disease The presence of calcareous plaques in the pericardium is noted frequently This always suggests a constricting pericardium, but calcium may occur in the pericardium without other findings of constrictive pericarditis

In the 24 cases reported by Harrington, the operative mortality was 25 per cent Of the 18 patients who recovered from operation, 9 were considered cured in the sense that subjective symptoms were relieved and the patient was able to resume his former occupation or to engage in some other useful one. The improvement in 2 more cases had approximated a cure In 2 other cases in which operation was recent, improvement had been progressive Thus, 13 of the 24 patients may eventually be considered as cured Of the remaining 5 patients who recovered from the operation, 2 had shown moderate improvement and 3 had died Two of these deaths were due to continuation of the disease, and 1 was due to pneumonia

A vexatious problem that continues to confront

the thoracic surgeon is the one presented by the patient who has the symptoms of progressive cardiac compression resulting from active tuberculous pericarditis The evidence that has accumulated in recent years suggests that in many cases constrictive pericarditis is caused by tuberculosis, but in many cases of tuberculous pericarditis, after the subsidence of the effusion, the onset of progressive compression of the heart becomes evident while the tuberculous lesion is still active, and long before the patient may be considered to have chronic constrictive pericarditis Under these circumstances, if operation is undertaken, a grossly thickened pericardium may be resected, but of necessity a layer of organizing fibrinous exudate is left adherent to the epicardium, and little if any improvement results I have recently had such an experience Partial pericardiectomy was successfully performed, but after a slight transitory improvement the patient died six weeks after operation from a continuation of her disease Operation was performed with reluctance, and only because the patient was progressively going downhill, although the cardiac-pericardial shadow was becoming smaller

Blalock and Levy<sup>27</sup> discussed a series of these patients a few years ago and came to the conclusion that one should operate only when it appears that the patient will die if something is not done Beck<sup>28</sup> is of the same opinion

### CONGENITAL DEFICIENCY OF THE PERICARDIUM

Rusby and Sellors<sup>29</sup> describe a case of partial deficiency of the pericardium associated with a solitary bronchogenic cyst, both on the left side, in a girl of ten Eighty such cases have been reported in the literature, but this is only the third case to be recognized during life, and the only one to be carefully studied at operation Uneventful recovery followed removal of the cyst. The authors believe it likely that partial left-sided deficiency of the pericardium is due to abnormal development, with premature atrophy of the left duct of Cuvier

### OTHER INDICATIONS FOR PERICARDIOTOMY

After enumerating the standard conditions demanding pericardiectomy, Neuhof<sup>30</sup> suggests its employment for various other conditions, some of which were encountered in the course of thoracic operations undertaken for noncardiac lesions

In a number of cases of carcinoma of the lung, there was considerable doubt at exploratory thoracotomy regarding the extent of hilar-node involvement, particularly so when the lung was broadly adherent posteriorly and when the tumor in the lung abutted on the posterior mediastinum Pericardiectomy and exploration within the sac supplied the information In another case, a carcinoma of the lung at first appeared to be inoperable because of fixation at the mediastinum and invasion of the pericardium Exploratory pericardiectomy revealed

the extent of the invasion, and liberal sacrifice of the pericardium permitted successful pulmonary resection. I have used this maneuver on several occasions for similar indications and have found it useful.

In the discussion of Neuhof's paper, Haight<sup>31</sup> cited a case in which he resected a large segment of the pericardium so that he might successfully perform pneumonectomy for a bronchogenic carcinoma that was invading the pericardium. Troublesome herniation of the heart resulted in shock if the patient lay on his back or on the operated side postoperatively. It was necessary to keep the patient inclined toward the contralateral side for some days after operation, but eventually he became stabilized, and three years after operation he showed no evidence of cardiac embarrassment.

Neuhof<sup>30</sup> also suggested incision of the pericardium and retraction of the pulmonary artery mesialward in cases of patent ductus arteriosus complicated by subacute endarteritis, so as to facilitate exposure of the deep surface of the ductus. Jones,<sup>32</sup> however, believes that there is a disadvantage in opening the pericardium in these cases, because the trickle of pericardial fluid obscures the field of dissection.

Graham<sup>33</sup> briefly describes the case of a woman who had a recurrence of a carcinoma of the breast in the pericardium, with massive bloody pericardial effusion that required frequent tapping. By the simple procedure of removing some of the pericardium and permitting the recurring effusion to drain into the left pleural cavity, the patient was

kept perfectly comfortable for a period of two years, when she died of further recurrences. Graham emphasizes the simplicity of the procedure and the great comfort that it gave to this patient.

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

#### CASE 32161

##### PRESENTATION OF CASE

A forty-one-year-old truck driver entered the hospital because of a mass in the left upper quadrant of the abdomen.

Five months before admission the patient was referred to the Out Patient Department for study of an albuminuria that had been discovered during an examination for life insurance. In the clinic his urine was repeatedly negative for albumin, although a trace was found on one occasion. A hard, movable mass was found in the left upper quadrant that extended from near the midline into the left flank and from the costal margin downward for 8 cm. It was nontender and moved with respiration. It had not caused symptoms. The liver border was palpated 3 cm below the rib margin and was separate from the mass. There were external hemorrhoids, but no visible abdominal veins. Examination of the blood was normal except for a slight eosinophilia (8 per cent). X-ray examination revealed a large soft-tissue shadow overlying the left kidney and displacing it somewhat laterally. The spleen looked normal. There was distortion of the superior calyx of the left kidney following an intravenous pyelogram, but owing to the obscuring shadow, this was by no means definite. A barium swallow failed to indicate esophageal varices. The blood nonprotein nitrogen, total protein and albumin-globulin ratio were normal. Bromsulfalein excretion was normal, and the cephalin-flocculation test was negative. The only significant facts in the past history were that he regularly consumed a half pint of whisky every two days. He had never been out of this country. The patient refused immediate operation.

About four months later he began to have occasional slight, nonradiating pains in the region of the mass, lasting from two to three minutes each. He then entered the hospital for operation.

The physical findings were not changed. Examination of the blood showed 4 per cent eosinophils and was not otherwise remarkable. The urine gave a ++ test for albumin, and a concentration test showed a maximum specific gravity of 1.018. A gastrointestinal series demonstrated a large pressure defect in the lesser curvature caused by a mass that

displaced the stomach laterally, downward and forward (Fig 1), the ligament of Treitz was displaced, but there was no deformity of the duodenum. A barium enema was negative. A cholecystogram showed the gall bladder to be normally outlined. There was no blood in the stool.

An operation was performed on the fifteenth hospital day.

##### DIFFERENTIAL DIAGNOSIS

DR WALTER GARREY: Apparently this man was machine-processed in an insurance examination in which a urinalysis was done before a complete physical examination. Albumin was found in the



FIGURE 1

urine, and he was then sent to the Out Patient Department, where physical examination showed a hard movable asymptomatic mass in the left upper quadrant. Perhaps this would be a good time to see the x-ray films.

DR JAMES R LINGLEY: This is a plain abdominal film showing the mass, which fills almost the entire left upper abdomen. This is a pyelogram showing rather poor filling of the pelvis and calyces on the left side, probably due to pressure from the mass rather than to intrinsic involvement of the kidney. One can trace the kidney shadow through the mass.

quite easily. The colon shows no evidence of intrinsic disease, although the splenic flexure is displaced laterally and somewhat posteriorly by the mass. The gastrointestinal examination shows this large pressure defect on the lesser curvature of the stomach, which involves practically all the lesser curvature and has caused marked displacement of the stomach toward the left. The mucosa over this area looks normal, in other words, I can see no evidence of actual mucosal invasion. The chest plate is negative.

DR GARREY: I had three questions to put to Dr Lingley, he has already answered two of them. One was whether the kidney outline was visualized and was entirely separate from the mass. It was. The second question was whether the mucosal pattern was seen clearly down the entire length of the mass. It was. The third was whether there was any calcification in the mass.

DR LINGLEY: There is none.

DR GARREY: I am afraid that we do not get much help from the x-ray studies. There was a mass, but I am not even sure what organs were involved. The mass was contiguous to the kidney, liver, spleen, retroperitoneal tissues and root of the mesentery. According to the symptoms, it was increasing in size rather slowly. I cannot imagine any infectious process that would behave this way, with the possible exception of hydatid cyst. This man had not lived in Iceland or the Antipodes, and despite the slight eosinophilia, I do not believe that we can hazard such a diagnosis. The picture certainly does not fit that of a syphilitic liver, so I think we have to assume that the mass was on a congenital or neoplastic basis. Apparently the men in the Out Patient Department thought that the patient possibly had cirrhosis and that the mass might have been derived from the liver, perhaps a primary liver-cell neoplasm. The majority of hepatomas and cholangiomas arise in a cirrhotic liver, I think the figure is around 85 per cent. Is that correct?

DR TRACY B. MALLORY: Around here.

DR GARREY: But we have no evidence of cirrhosis. As a further interesting exercise in trying to arrive at a diagnosis, a peritoneoscopy might have been done and even a gastroscopy. A peritoneoscopy probably would not have shown the tumor directly, since it appears to have been located behind the stomach and lesser omentum and mesocolon.

DR MALLORY: A peritoneoscopy was done. Would you like to have the information?

DR GARREY: Peritoneoscopy would be worth while on the remote chance that this man had dissemination of a neoplasm and also to rule out the liver disease, but I venture to guess that it was not helpful in telling anything about the primary tumor.

DR MALLORY: The gall bladder was visualized. The peritoneal cavity appeared normal, except in the left upper quadrant, where a mass could be

seen just to the left of the greater curvature, between it and the spleen. The latter could not be visualized. The mass had a grayish-blue tinge, was covered with thin omentum and appeared to be cystic. It was not attached to the abdominal wall. There was no lobulation.

DR GARREY: Very wisely no biopsy was done, since if it were a cystic mass they did not want to spill material freely into the peritoneal cavity. I am very much interested in the physical finding of mobility, which makes the diagnosis all the harder to me. They speak of the mass as being movable in the first examination, and also that it moved with respiration, and again in the examination in the hospital four months later they mention that the mass was movable. The most probable mass in this area that has this characteristic position, size and symmetry is a cyst of the pancreas. We get no lead from the history. There was no trauma, and no biliary tract disease, which might have predisposed to a pseudocyst. A rather small percentage of pancreatic cysts are movable. The nearer they are to the tail of the pancreas and the more ptotic the patient, the likelier the mobility. Pancreatic cyst seems to be a strong possibility, although the patients with pancreatic cysts whom I have seen have had more pain than this man appeared to have, provided that the tumors had reached this size. I assume that the albuminuria was due to pressure on the left renal vein and kidney. This has been reported in an occasional case.

I do not believe that we are dealing with a particularly malignant situation because the man had no constitutional symptoms or signs. He did not appear to have run downhill after this five-month period. If he had a solid neoplasm of a disseminating, highly malignant character, I should expect that some other finding would have been manifest by this time. I do not believe that, with the mobility that they have emphasized, a retroperitoneal neoplasm, a sarcoma, is likely, or a large fibrosarcoma. This does not appear to have had the character of a lymphomatous tumor; it was not nodular, and it appeared symmetrical and cystic, both in the x-ray films and at the time of peritoneoscopy. There are rare tumors that may arise in the space behind the stomach—hemangioendothelioma, dermoid cyst, a cyst containing sebaceous material and tumors of neurogenic origin. I am driven away from virulent neoplasm and incline more and more to the supposition that this was a relatively benign lesion occurring in tissue at the root of the mesentery or possibly in the pancreas. Fifteen days were spent in studying this man in an attempt to make a diagnosis. They also were groping for any concurrent disease that might have given a lead to the diagnosis, but they wisely ruled it out.

My first hunch is pancreatic cyst, either a pseudocyst or a cystadenoma. My second hunch is some

are but relatively benign tumor occurring in the same area, possibly a cyst of congenital origin high in the mesentery, although the location was higher than it usually is in cases of this sort. I think that they probably had to end up by doing what is recommended by one of the late Dr G W W Brewster's dictums, which some of you may remember. He urged, that if one found trouble, to cut over it.

DR. MALLORY Dr. Volwiler, you studied this patient on the ward. Have you any comment?

DR. WADE VOLWILER I saw him with the third-year medical students in the Out Patient Department, and we reached no definite decision. We thought that the likeliest diagnosis was pancreatic cyst.

DR. CLAUDE E. WELCH It took Dr. Garrey only twenty minutes to make the wrong diagnosis, but it took us over two weeks. The albuminuria, which Dr. Garrey was somewhat interested in, turned out to have no significance. So far as the tumor was concerned, we thought that it was a pancreatic cyst, because it was somewhat spherical and therefore probably represented encysted fluid rather than a solid tumor. On entering the abdomen we found that this was a solid tumor tightly attached to the wall of the stomach. As a matter of fact it was impossible to separate the stomach from the tumor. There was no attachment elsewhere. We therefore had to proceed with a subtotal gastric resection. We sent for a pathologist to look over the specimen as soon as it was removed, because we were interested in the fact that large, probably hyperplastic, lymph nodes extended up the left gastric artery. We wanted to be sure that the line of resection, which was close to the esophagus, was free of disease. The pathologist's opinion was that it was a benign tumor.

#### CLINICAL DIAGNOSIS

Cyst of pancreas

#### DR. GARREY'S DIAGNOSIS

Cyst of pancreas

#### ANATOMICAL DIAGNOSIS

Neurinoma of stomach.

#### PATHOLOGICAL DISCUSSION

DR. MALLORY The tumor was a benign spindle-cell tumor of the stomach. There might be some argument whether to classify it as a leiomyoma or as a perineurial fibroma. I personally believe that it was the latter. Its apparently cystic character was due to extreme vascularity. It was so vascular that when we first saw the section the possibility of angioma suggested itself to our minds. There was no extension of the tumor beyond the point of actual attachment to the gastric wall, and I think that there is no question that cure has been achieved.

DR. WALTER BAUER In retrospect, would the radiologist interpret the films any differently?

DR. LINGLEY I should still think that it was a pancreatic cyst.

### CASE 32162

#### PRESENTATION OF CASE

A fifty-year-old man entered the hospital because of stomach pain.

Fourteen months before admission the patient first began to have crampy midepigastic pain that came on three or four hours after each meal. He consulted his physician, who obtained a gastrointestinal series that was said to have demonstrated a stomach ulcer. He was put on a liberal, low-fat, bland diet and given "powders and white liquid" to take between meals. On this regime he obtained almost complete relief for seven or eight months, when he had a recurrence of postprandial pain, which persisted despite the powders but was relieved by food. One month before admission he had another gastrointestinal series, following which he was told that he would have to have his stomach removed. He belched frequently and felt epigastric fullness and vague uneasiness after meals. On a few occasions he induced vomiting because of distressing fullness. The bowel movements were regular. No bloody or tarry stools were noticed.

The physical examination was negative except for a walnut-sized indirect inguinal hernia.

The temperature, pulse and respirations were normal, the blood pressure was 110 systolic, 70 diastolic.

The hemoglobin was 15.8 gm per 100 cc. The urine was normal. A gastric analysis showed no free hydrochloric acid in the first specimen, and 27 and 15 units, respectively, in the second and third specimens.

X-ray examination of the stomach showed a marked degree of spasm of the antrum. At the mid-portion of the lesser curvature there was a shallow collection of barium, which might have represented a flat crater. The first portion of the duodenum was constantly deformed at its apex, no crater was found in that region. There was a 1-cm diverticulum projecting medially from the second portion of the duodenum. The heart and lungs were normal by x-ray examination.

An operation was performed on the fifth hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR. WADE VOLWILER I infer that this man was moderately obese, since the only reason for giving a low-fat diet to a patient with simple ulcer is to avoid a gain of weight during a program of frequent feedings.

The center of interest here lies in the identity of this vague questionable lesion in the lesser curvature, and I think that we should have 'an x-ray opinion first. I should like to ask several specific questions. Can we assume that this duodenal deformity represents the crater of a benign ulcer at some time in the past? Can this vague lesion in the lesser curvature be interpreted in one of three ways—a scar following the healing of an ulcer in that area, a flat shallow crater or just a collection of barium between hypertrophied gastric rugae?

DR JAMES R. LINGLEY: I did the examination on this particular patient, and those were the exact questions that I had in mind while doing it. I had great difficulty in determining whether or not this lesion in the lesser curvature was a crater. The most remarkable thing about the stomach was the extreme spasm of the antrum. Trying to find some cause for the spasm, I studied the area on the lesser curvature extremely carefully and found a lesion 1.5 cm. in size where the barium tended to puddle out and form a shallow crater.

DR VOLWILER: Was there rigidity over that area?

DR LINGLEY: That was difficult to determine because the stomach was high, lying under the costal border, and we could not palpate it. There was no peristalsis in that region. I thought that it was a crater, probably an extremely shallow one, representing an almost healed ulcer. The patient showed a constant deformity of the apex of the duodenum and a small diverticulum in the second portion.

DR VOLWILER: The duodenal picture probably represents the healed stage of a benign ulcer.

Let us go back to the present illness, which began with the typical symptoms of peptic ulcer, and which disappeared almost completely in eight months on a fairly satisfactory ulcer regime. I am going to assume that during that time the original ulcer had healed almost completely, if not completely. We do not know where the ulcer was, but it could have been either a duodenal or a gastric ulcer. I think that we should take the patient's statement at face value and assume that it was a gastric ulcer and that it had probably originated at the site of the present defect. During the two months before entry there was a sudden change of symptoms, which is significant. Diffuse hypertrophic gastritis could have produced the recent symptoms of this man and might have been difficult to demonstrate by x-ray. It can occur in a localized form, but it is seldom observed on the midportion of the lesser curvature and the localized form usually does not give rise to such extensive symptoms. I believe that the development of such a process, leading to the symptomatology that existed here during the time that the patient was following a fairly good regime, is highly unlikely, and I therefore shall dis-

card it. I shall also discard a scar as an explanation of the lesion, because that, of course, could not explain the symptoms.

We should perhaps mention cholecystitis, cholelithiasis and even subacute recurring mild pancreatitis as an explanation of the symptoms. There is no evidence for them, however, and we should focus our attention on the stomach. I am not sure whether there was an ulcer crater. But regardless of that fact, I think that, in view of the symptoms, the most logical explanation for the lesion is a small, slowly growing, infiltrating carcinoma. I say that in spite of the facts that this patient probably was moderately obese, that he had previously had a benign lesion in the duodenum, that the stomach produced free acid and that the x-ray defect was questionable. This patient certainly should have been operated on. A preoperative gastroscopy might have given valuable information, but regardless of what was found, I believe that the stomach should have come out. This may have been one of those occasional extremely difficult cases in which neither the surgeon nor the pathologist on gross examination can decide what the lesion is. It may have been only the microscopical examination that revealed the true identity of the lesion.

#### CLINICAL DIAGNOSIS

Gastric ulcer

#### DR VOLWILER'S DIAGNOSES

Carcinoma of stomach  
Old benign duodenal ulcer

#### ANATOMICAL DIAGNOSIS

Carcinoma of stomach

#### PATHOLOGICAL DISCUSSION

DR TRACY B. MALLORY: The patient was operated on, and a subtotal gastric resection was performed. We found on the lesser curvature a localized area, slightly over 2 cm. in diameter, where the mucosa appeared thicker and firmer than elsewhere, with a somewhat different translucence and color, at one margin there was a shallow erosion. The wall of the stomach was thickened and indurated under this area of altered mucosa. The gross appearance, however, was essentially that of a healed ulcer rather than of a neoplasm. When the microscopic preparations came through it became evident that the entire area of altered mucosa showed a carcinoma in situ. At one single spot tumor cells had invaded the submucosa, and two or three glands had penetrated a short distance into the muscularis. Several small lymph nodes were examined. All were negative, as one would expect with such an early lesion.



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## THE INADEQUACIES OF MEDICAL CARE

### II THOSE CONCERNING ITS DISTRIBUTION AND COST

OF UTMOST interest at the moment in matters pertaining to medical care are its distribution and cost. It is a well recognized fact that many persons fail to receive adequate medical care either because it is unavailable or because they are of the opinion that they cannot afford it. At times this is inexcusable, since the means are at hand provided that the person knows how to obtain them. On the other hand, in the majority of cases there is a just complaint. In many areas facilities are lacking, in others they are inadequate, and in all certain fees for medical care are out of all proportion with the income of the patient.

Obviously legislation should be directed toward the relief of sections that lack facilities for medical

care. Hospitals and health centers should be constructed and equipped by the state, with the assistance of federal grants-in-aid, and these in turn would have a tendency to attract properly qualified physicians. To be sure, the economic status of any particular section may be such that the physician is unable to obtain a living wage, but that again is a responsibility of the state, which should guarantee a reasonable income by supplementing what he is able to earn with a salary or retaining fee.

Inadequate care involves poorly trained physicians, those who had proper training but have failed to keep up with medical advances, a scarcity of qualified specialists and lack of proper hospital facilities. The first two concern the quality of medical care and the last has to do with hospital rather than medical care, all of which will be discussed in subsequent editorials. Lack of well trained specialists in any given section is largely a matter of insufficient incentive for the specialist to practice there, physicians of this type naturally tend to congregate in large or moderate-sized cities, where well equipped hospitals are located and where they are satisfactorily paid for their services either by salaries or by fees. To persuade them to settle in sparsely settled areas or in those of low economic status again will require state aid.

The matter of cost of medical care naturally receives the topmost attention from the public. By and large, the indigent, particularly those who reside in or near urban areas, now receive reasonably good medical care with little or no cost, and those with low to moderate incomes are capable of handling the expense of minor illness with slight financial inconvenience. But the consequences of a major medical or surgical illness, including loss of wages, is a catastrophe for which few of the latter group have provided.

No doubt much needs to be done to improve the medical care of the indigent in areas other than urban. Many of the handicaps to this type of care would be removed if hospitals and health centers were made available, the cost being met by state funds, with the assistance of federal grants-in-aid.

A great deal has been written concerning the high cost of medical care. There is no doubt that this expense has risen tremendously in recent years, but

so, too, has that for almost everything else. On the other hand, what appear to be large fees do not necessarily mean a high net income to the physician. His training, particularly if he is a qualified specialist, represents a considerable capital outlay, which often must be repaid over a period of years, furthermore. His actual cost of successfully practicing medicine is many times larger than that of the old family doctor. Hospitalization and expert nursing care also add appreciably to the expense of a serious illness, but no one can deny that the patient who is obliged to undergo a gastrectomy is better off in a modern hospital than he would be if he were operated on lying on a door in the kitchen or back parlor. No doubt the cost of serious illness has risen, nor does there seem to be any logical way in which it

can be appreciably lowered in any individual case. All of which means that persons in the low-income group and even in the moderate-income group must set aside money in anticipation of catastrophic illness. In other words they must insure against it just as they insure against fire or burglary. Compensation for loss of wages due to illness might well be included among the benefits provided by the Social Security program.

It seems likely that the cost of good medical care can be lowered by group practice. In the obscure case, the opinions of various specialists can obviously be obtained for less actual cost and with less inconvenience to the patient if these men have banded together in a group than if they are practicing as individuals. Outstanding examples of this type of organization are the nationally known large private clinics and those connected with teaching hospitals, and there are hundreds of small groups scattered throughout the United States, particularly in the Mid-West and South. This type of practice has much to offer, and it will probably become

more popular in the near future than it has been in the past.

In summary, the inadequacies of the distribution of medical care are largely the concern of government, although ignorance of the public concerning available facilities is far from a negligible factor. The high cost of medical care can undoubtedly be somewhat lowered by group practice, but there

appears to be no way of eliminating the expense of catastrophic illness, other than by insuring against it.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

### TEACHING HOSPITALS

IN A recent address, Dr. Alan Gregg,<sup>1</sup> director for the medical sciences, Rockefeller Foundation, discussed the place of the teaching hospital in the training of medical students and nurses, for

the specialized and advanced training of physicians and for the advancement of medical knowledge. In addition, he emphasized what may be of equal or even greater importance to the public who supports these hospitals, namely, that the teaching hospital provides the best type of care for the patient. In speaking about the patients whose cases are studied by medical students and their teachers, Dr. Gregg said in part:

What an amazing misconception about this procedure is rampant among most laymen! They think that when they consent to be part of a demonstration in a clinic, for teaching purposes, they are conceding something of their comfort and well-being to the professional zeal of young doctors. The exact opposite is true. When a patient consents to this procedure, his case receives the most careful, the most accurate and most modern treatment. Actually, it has all the advantages of an early consultation. So few people understand this. So many, especially of the middle class income group, ought to realize this. They should know that to consent to be used for teaching is to display the most enlightened self-interest.

In a comment on President Truman's special message to Congress advocating compulsory national medical insurance, the Committee on Medicine and

the Changing Order of the New York Academy of Medicine<sup>2</sup> made some pertinent suggestions. To raise the quality and to round out the scope of medical care extended under any system of payment, the committee favors not only a number of revisions in medical education but also the gradual extension of group practice. In this connection, it is stated

It is essential, moreover, that medical group practice units be organized also in relation to teaching hospitals, since an extension of prepaid medical care to all people of low income must inevitably have important repercussions on medical education and research. The medical schools, for their part, must change their methods if they are to train doctors for a new form of medical care, and no form of medical care can afford to neglect the advantages to the patient of teaching and research.

That the teaching hospital must provide the best type of medical care for the patients can readily be appreciated on the briefest reflection. The patient whose case is used for teaching *must* receive the best of modern care. Everybody from student through intern and resident to visiting physician must be on the alert and aware of the up-to-date methods of diagnosis and treatment. The alternative is to lay oneself open to censure or to lose dignity and respect.

Perhaps the greatest possibilities for abuse by the medical profession exist in the practice of surgery or of the surgical specialties. In small hospitals and in strictly private hospitals, or even in the large public hospitals, if there is not a feeling of responsibility on the part of the surgeon to justify every step, and also the willingness on his part to take the time and trouble to keep in touch with medical progress, the patients suffer. This, however, is not limited to surgeons. One can readily imagine the abuses that are possible in the care of neuropsychiatric cases by unscrupulous physicians when the management of their cases is not subject to review and justification.

The Veterans Administration, in its recent reorganization, has accepted the concept of the teaching hospital as the only available means of establishing and maintaining the highest quality of medical service. Teachers from medical centers are to be chosen to staff its hospitals on a part-time basis. They are expected to provide the incentive for the resident staff to study their cases adequately,

so as to be able to provide the best of medical care. The close association of interns and residents with these teachers will also provide inspiration to the younger men to sustain interest, to follow their cases closely and to correlate their findings and thus be in a position to improve and advance the quality of service that they offer.

In hospitals whose staffs are not closely allied with medical schools, promotions within the staff are based entirely on seniority. It is obvious that when such promotions are made without considering the professional qualities and attainments of the physician the quality of the care that the patients receive is apt to suffer. Naturally, those who would otherwise rise by seniority rather than by attainment are likely to resist any attempt by medical schools to deprive them of their rights to promotion. The sole duty of medical schools is to provide good clinical instruction, and this predicates the best medical care for the patient and the choice of the persons best qualified to give such care. Thus, resistance to change was undoubtedly met by the new heads of the Veterans Administration when many of the less qualified among the senior officers had to be replaced.

Administrators and trustees of public hospitals and their medical staffs would do well to take the cue from the Veterans Administration. Needless to say, the least qualified among the staff members will be relegated to less responsible positions when a medical school affiliating with a hospital is given a free hand in the selection of teachers and a determining role in promotions within the staff. When a hospital staff resists such a move as an encroachment on its prerogatives, it is paramount to an admission either of inferiority or of a lack of interest on the part of its members. In other words, such an attitude must be interpreted as indicating either that they are unsuited for the positions or that they are not sufficiently interested in the welfare of their patients and of the hospital and in the improvement of medical practice to take the time and to put in the extra effort that is required of the members of the staff of a teaching hospital.

Both the hospital and the medical school have added responsibilities when they become affiliated, and these all accrue to the benefit of the patient.

The hospital must provide the facilities for the best of medical practice, and these are always under the scrutiny of the students and their preceptors. The latter must always be on their toes and keep up to date. Medical schools, on the other hand, have the responsibility of seeing that they make the best choice and that they recommend promotions solely on the basis of merit and achievement.

### REFERENCES

- 1 Gregg, A. Trends in medical education. A chapter in *The Doctors Talk It Over*. Vol II. New York: Lederle Laboratories, Incorporated, 1945.
- 2 Statement. Medicine and the changing order. *J A M A* 130 94, 1946.

## MASSACHUSETTS MEDICAL SOCIETY

### ANNUAL MEETING OF THE COUNCIL

The annual meeting of the Council will be held in the Georgian Room of the Hotel Statler, Boston, on Tuesday, May 21, 1946, at 7 00 p m. This meeting will be preceded by the Cotting supper which will be served in Parlors A and B of the same hotel at 6 00 p m.

#### Business

- 1 Presentation of record of the stated meeting of the Council held February 6, 1946. To be published in the *New England Journal of Medicine*, issue of May 2, 1946.
- 2 Reports of standing and special committees.
- 3 Election of officers and orator.
- 4 Appointment of committees for ensuing year.
- 5 Such other business as may lawfully come before the meeting.

MICHAEL A. TIGHE, *Secretary*

## SUBCOMMITTEE ON VETERANS' AFFAIRS, POSTWAR PLANNING COMMITTEE

In the course of its investigation of the needs of medical officers who had returned from the armed forces, the Subcommittee on Veterans' Affairs soon stumbled on the serious problem of early telephone listing for doctors reopening their offices. The committee pursued this subject as soon as possible in order to get early action thereon. A preliminary report of the committee's findings is as follows:

The next telephone directory will be published for the Boston District in December. Owing to the paper shortage this is the earliest date that the Government will permit publication of a new directory. The New England Telephone and Telegraph Company is fully aware of the seriousness of this problem, not only for doctors but also for other professional men. It has canvassed means to solve it and has taken the following steps:

- (1) A leaflet will accompany the April telephone bills urging subscribers to make use of Information Service for numbers that they cannot find and pointing out that since the last directory was published there has been a gain of 72,000 phones in the Boston area (225,000 in the total area served).

(2) It has expanded Information Service and is continuing this expansion as fast as new operators are trained. In the Boston area there will eventually be an increase of 15 per cent (128 operators) in the personnel of this service.

(3) Beginning about April 1, the company will stress the use of Information Service in advertising especially in the daily papers. This will be a regular campaign and the company accepted the suggestion to stress the use of this service in the advertising in connection with the phrase "your doctor" or "your attorney who has returned from the services."

(4) The company welcomes any suggestion as to how to make doctors' numbers more readily available to the public, subject to the limitations outlined above. At the present time every number is in the hands of Information Service within twenty-four hours of the installation of the telephone.

(5) Doctors can help this campaign by telling their patients to use Information Service for numbers they fail to find in the directory.

The company has been most courteous and patient and has explained to us in detail many of the difficulties involved and the reasons that led them to adopt this as the only solution to the present dilemma.

G. PHILIP GRABFIELD, *Chairman*

## TREASURER'S REPORT COVERING REFUND DISTRIBUTION

The Treasurer of the Massachusetts Medical Society makes the following report regarding the refund to district societies for 1946:

The Council voted to distribute the sum of \$4000 to district societies. The total number of payments of annual dues received by the Treasurer by March 1, to be counted for the refund, was 3965. Therefore the refund to the district societies for each paid fellow is \$1.009.

The following table gives the number of payments, as of March 1, and the refund to each district as of April 1:

DISTRICT	NUMBER REPORTED PAID	REFUND
Barnstable	39	\$39.12
Berkshire	104	104.88
Bristol North	57	57.48
Bristol South	155	156.36
Essex North	150	151.31
Essex South	217	218.91
Franklin	35	35.29
Hampden	260	262.30
Hampshire	61	61.51
Middlesex East	114	114.99
Middlesex North	102	102.88
Middlesex South	810	817.25
Norfolk	699	705.26
Norfolk South	107	107.92
Plymouth	114	114.99
Suffolk	532	536.75
Worcester	332	334.95
Worcester North	77	77.65
-	3965	\$4000.00

In 1945, for comparison, the total number of payments for the refund was 3297.

ELIOT HUBBARD, JR., M.D., *Treasurer*

## MEDICOLEGAL ABSTRACT

**Relation of Patient and Physician Liability for malpractice.** The plaintiff alleged that the defendant, a dentist, had broken off a drill and hypodermic needle in his jawbone, that these were the cause of his illness and considerable medical expenses to which he had been put, that the defendant knew that the drill and the needle were there and

that he had fraudulently concealed the facts from the plaintiff

The defendant made a motion to dismiss by reason of the acts having taken place more than two years before the suit was begun

The Arizona court held that the dentist had a duty to disclose the facts to the plaintiff and that his failure to do so was such fraud as to prevent the running of the Statute of Limitations until the facts fraudulently concealed became known — (*Acton Morrison*, 155 Pac [2d] 782, Jan 29, 1945, Arizona)

This case may be distinguished from a Massachusetts case in which it was alleged that the defendant, physician, left gauze in the plaintiff during an operation performed more than two years before the action was brought. The gauze was not discovered until shortly before the suit was begun. There was no allegation that the doctor knew the gauze had been left in. The Supreme Judicial Court holding that the action was barred by the Statute of Limitations said that there was no showing that the defendant had fraudulently concealed the facts — (*Capucci v Barone*, 266 Mass 578 [1929])

It is noteworthy that the court in the first case considered the relation of dentist and patient such fiduciary relation that a mere failure to disclose without any affirmative act of concealment was sufficient to constitute fraud

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### CURED CANCER CLINICS

At the moment, fourteen Cured Cancer Clinics are scheduled to be conducted during the month of April. These clinics represent a special form of teaching clinic in which only cured cases will be shown. Such teaching clinics, held at the places of meeting of the regular state-aided cancer clinics, are designed for the purpose of advising the physicians of the community regarding cancer, its symptoms, diagnosis and treatment.

The clinics will be held at Beverly, Boston (Boston Dispensary and Beth Israel Hospital), Brockton, Fall River, Fitchburg, Gardner, Greenfield, Lawrence, New Bedford, Salem, Westfield (State Sanatorium), Worcester and Wrentham (Pondville Hospital).

Information regarding the dates and times of the Cured Cancer Clinics will be provided at the regular state-aided cancer clinics or at the local district health offices

## MISCELLANY

### NEW PSYCHIATRY PROGRAM AT BOSTON UNIVERSITY

With the appointment of Dr William Malamud as professor of psychiatry and chairman of the Department of Psychiatry at Boston University School of Medicine, the University will undertake a program of undergraduate instruction in this field that will meet the need for providing medical students with a more extensive training

In making the announcement of the appointment of Dr Malamud, who is now director of research at the Worcester State Hospital, President Daniel L. Marsh said that the School of Medicine has recognized for a long time that the psychiatry training offered today to students in medical

schools is generally inadequate. An anonymous gift of \$30,000 from a long-time friend of the University has now made possible the expansion of this part of the school's instructional program

Under the direction of Dr Malamud, the University will inaugurate a program of undergraduate training in psychiatry that will be carried on throughout all four years of the medical-school course. Special emphasis will be placed on giving the students an increased opportunity to receive training in the diagnosis and management of the neuroses, which are now recognized as constituting a large part of all medical practice

## CARE OF NONSERVICE-CONNECTED ILLNESS

Treatment in private hospitals, at government expense, of male veterans whose illnesses are not service connected cannot be authorized by the Veterans Administration, according to officials of the Boston Branch Office of the Veterans Administration. The statement was made to correct misinformation among both veterans and private-hospital authorities. Veterans whose disabilities are service connected may receive private-hospital treatment at government expense. Except in emergency cases, however, the veteran must make arrangements for such private-hospital care with the Veterans Administration prior to entering the institution.

In discussing nonservice-connected cases, the officials point out that arrangements may be made for treatment of women veterans in private hospitals at government expense if Veterans Administration hospital facilities are not available. Male veterans with nonservice-connected illnesses may be treated at Veterans Administration hospitals at government expense if beds are available in addition to those required by veterans whose disabilities are service connected

## BOOK REVIEWS

*The Diagnosis and Treatment of Acute Medical Disorders* By Francis D Murphy, M.D. 8°, cloth, 503 pp., with illustrations. Philadelphia: F. A. Davis Company, 1944. \$6.00

There are acute episodes and emergencies in medicine as well as in surgery. The disturbing problem that confronts the physician in such acute cases is one of correct diagnosis, the rest of the battle is to follow a certain routine treatment. In this book Dr Murphy has grouped a number of such emergencies under various headings and has dealt with them masterfully. It is really a volume on differential diagnosis, although the treatment in each case is not neglected. But it is the former that presents the major problem — things are not always what they appear to be on the surface.

The discussions in general are well presented and adequate. In a few places they appear to lack somewhat in detail, but some curtailment was undoubtedly necessitated for the sake of brevity. A great deal of material and up-to-date information has, however, been crowded into this volume. Some of the discussions on differential diagnosis are excellent for clarity and presentation and reveal the true teacher. Unfortunately, for the book-buyer, medical progress is so rapid that often by the time a volume is published new treatments and remedies have come to light, for example, in the treatment prescribed for subacute bacterial endocarditis, the author does not include massive doses of penicillin, for which recent reports claim great promise. Even in this day of refresher courses, here is a valuable volume that is stimulating and refreshing.

*Medical Care and Health Services for Rural People. A study prepared as a result of a conference held at Chicago, Illinois, April 11-13, 1944.* 8°, paper, 226 pp., with 12 charts. Chicago: Farm Foundation, 1944. Single copies, each \$1.00, five or more copies, each 60 cents.

This book is the report of a conference held at Chicago on April 11-13, 1944, which was sponsored by the Farm Foundation for the purpose of discussing medical care and health services for rural people. Representatives of many farm organizations, governmental agencies, medical organizations, universities and voluntary organizations comprised

most of the discussant group. Every phase of the problem was given consideration. Views expressed were as divergent as the opinions of the participants.

A committee comprised of representatives of the Farm Bureau, the Farmers Union, the Grange, and the Southern Tenants in Farmers Union submitted the following recommendations:

- 1 That the governor of each state be asked to appoint a committee or commission to study the problems of rural health and medical care in the respective states
- 2 That farm organizations be encouraged to continue study and experimentation in the field of health service, drawing upon local and national professional and civic groups, such as the associations of hospitals, physicians, public-health organizations, medical colleges and other groups
- 3 That the foundation stimulate the establishment of scholarships for farm boys and girls who will study medicine and nursing and return to rural areas for practice
- 4 That the foundation establish a national committee on rural health by providing technical services and information and by inviting the national farm organizations to name representatives to serve on the committee

This book, with its large amount of information, should be of considerable interest to physicians studying medical economic problems.

*Medical Uses of Soap. A symposium.* Edited by Morris Fishbein, M.D. 8<sup>th</sup> cloth, 182 pp., with 41 illustrations. Philadelphia: J. B. Lippincott Company, 1945. \$3.00.

Erasmus Wilson in the middle of the nineteenth century popularized the bath by his writings for laymen on the care of the skin. Since then soap has become increasingly popular, and as one of the collaborators of this book states, "There is a trite maximum to the end that the per-capita consumption of soap is a yardstick of a nation's degree of civilization." When the busy dermatologist reviews his practice, however, and notes the large number of soap-sensitized individuals he has to treat, he wonders whether or not the per-capita consumption of soap in America is not too excessive, as a result of the propaganda of soap manufacturers.

This treatise on soap is timely but must be read rather carefully and weighed in the balance. As stated in the preface, a book of this type — written by a group of collaborators — is bound to have a certain amount of duplication. This is noted not only in the discussion but also in the illustrations. Instead of repeating illustrations, pictures of other dermatoses would have been more appropriate. The first few chapters on the chemistry of soap are excellent; in fact, the book is so well done that it is difficult to find fault.

A few over-statements might be mentioned, such as on page 63, where it states acne due to chlorinated compounds can be prevented and aided by soap and water. This does not agree with the reviewer's experience in treating such cases. With reference to page 69, most plating procedures, such as nickel plating, are done in acid baths. After reading the discussion on synthetic detergents on page 84, one would think that sulfonated oils were a distinct entity, whereas they are probably the commonest of synthetic detergents. These remarks are quoted merely to show what an excellent symposium this collection of articles forms. This is a book that should be read by everyone interested in soap, and should be a valuable addition to the library of the physician, the student and the layman.

## NOTICES

### ANNOUNCEMENTS

Dr. Robert J. Cataldo announces the opening of his offices for the practice of internal medicine at 820 Main Street, Waltham, and 475 Commonwealth Avenue, Boston.

Dr. Trygve Gundersen wishes to announce his return to the practice of ophthalmology at 101 Bay State Road, Boston.

Dr. Sumner D. Liebman announces his return from military service and the opening of an office for the practice of ophthalmology at 115 Bay State Road, Boston.

## MASSACHUSETTS PHYSIOTHERAPY ASSOCIATION

The Massachusetts Physiotherapy Association Incorporated, which is the Massachusetts chapter of the American Physiotherapy Association, will gladly furnish a directory of its members to any member of the medical profession. Requests should be addressed to Mrs. Dorothy V. Warren, Physical Therapy Department, Massachusetts General Hospital, Fruit Street, Boston.

## NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The regular spring meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary on Wednesday, May 8.

## AMERICAN COLLEGE OF CHEST PHYSICIANS

The next oral and written examinations for fellowship in the American College of Chest Physicians will be held at San Francisco on June 29. Applicants for fellowship in the College who plan on taking the examination should communicate with the Executive Secretary, American College of Chest Physicians, 500 North Dearborn Street, Chicago 10.

The twelfth annual meeting of the College is scheduled to be held at the Sir Francis Drake Hotel, San Francisco, on June 29 and 30 and July 1 and 2.

## BOSTON GASTROENTEROLOGICAL SOCIETY

A meeting of the Boston Gastroenterological Society will be held at the Harvard Club of Boston on Wednesday, April 24, at 12 m. Dr. Reginald Fitz will deliver an address on the subject "Appendicitis and Its Complications." Luncheon will be served free to members and a nominal charge will be made for guests. Reservations may be made by telephoning the secretary, Dr. C. W. McClure at KENmore 3200.

## MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS

The annual meeting of the Massachusetts Society of Examining Physicians will be held on Wednesday, May 8, in the Colonial Room of the Copley Plaza Hotel, Boston.

Dinner is scheduled for 6:30 p.m., to be followed by a round-table discussion of the Wagner-Murray-Dingell Bill, with Dr. Joseph S. Lawrence, chief public relations officer of the American Medical Association at Washington, D.C., and Dr. Allan M. Butler, of the Massachusetts General Hospital, as the chief speakers.

Because of the interest in the subject to be discussed, the society will welcome nonmembers who may wish to attend. Reservations for the dinner may be made by writing to Miss Anne Rodman, Assistant Secretary, 157 Fourth Street, Medford, Massachusetts.

## NEW YORK ACADEMY OF MEDICINE

The Nineteenth Graduate Fortnight of the New York Academy of Medicine will be held October 7 through October 18, the subject being "Tumors." The program includes evening lectures, morning panel discussion, scientific exhibits and demonstrations at the Academy and afternoon clinics at leading hospitals of New York City. Complete programs will be mailed to physicians on request.

A physician who is not a fellow of the Academy may secure registration by sending his name and address, accompanied by a check for five dollars, to the Secretary of the Graduate Fortnight Committee, 2 East 103rd Street, New York 29, New York. Medical officers of the United States Army, Navy and Public Health Service, on active duty, will be admitted to all sessions without a registration fee.

(Notices continued on page xvii)

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## THE PROBLEM OF NUTRITION IN THE POSTOPERATIVE CARE OF ABDOMINAL WOUNDS OF WARFARE\*

LIEUTENANT COLONEL J E DUNPHY, M C, A U S, MAJOR STANLEY O HOERR, M C, A U S,  
CAPTAIN C L DIMMILER, Jr, M C, A U S, AND CAPTAIN ROBERT R WHITE, M C, A U S

RAPID evacuation, the improved treatment of shock and skilled surgery available within a few miles of the front have made it possible to operate on many patients with abdominal wounds of an extent and gravity seldom seen in those treated in World War I. Despite this fact, the immediate postoperative mortality of 50 per cent, generally accepted as representative of the last war,<sup>1</sup> has been considerably reduced.<sup>2, 3</sup> Most reports of experiences in this field have dealt largely with the operative and immediate postoperative periods. The complex problems in nutrition and sepsis presented by some of these patients on arrival at fixed hospitals have not been emphasized.

During the campaign in Normandy, the normal channels of evacuation for postoperative abdominal cases by-passed this unit, which received only slightly wounded men who could be promptly returned to duty or seriously wounded ones whose condition was so precarious that evacuation to the United Kingdom was impossible. In the latter group were 16 patients gravely ill with extensive abdominal wounds. These patients were selected for transfer to this unit specifically because of their poor general condition, and represent only the more complicated end results in a series of about 150 cases.

The nature and severity of the injuries are significant (Table 1). There were multiple injuries in every case. The small bowel was perforated in 9 cases, the colon in 6 cases, and the rectum in 1 case. There were liver wounds in 3 cases, a duodenal wound in 1, and a gastric wound in 1. The bladder was involved in 2 cases and the urethra in 1. In 2 cases there were combined abdominal and thoracic wounds. Ten patients had extensive soft-tissue injuries, with buttock or perineal wounds in 6 of them. There were 7 cases of compound fracture, which involved the sacrum in 4 cases and the humerus, forearm and femur in 1 case each. One patient required a high amputation of the thigh because of destruction of the external iliac artery and vein. Resection of

the bowel had been necessary in 6 cases. In 1 of them, both the ileum and the colon had been resected, and in another, three separate resections of the small bowel had been performed.

### POSTOPERATIVE COMPLICATIONS

All 16 patients had varying degrees of anemia and hypoproteinemia when they reached this unit. There were 5 patients with external fistula, which involved the genitourinary tract in 3 cases and the duodenum and ileum in 1 each. Infection—retroperitoneal, peritoneal or in the wound—constituted a major complication in 12 cases. It was the cause of the 2 deaths in this group, in one case from rapidly progressing peritonitis and on the other from extensive retroperitoneal abscesses. Intestinal obstruction developed in 11 cases and required reoperation in 2 of them. There were 7 cases of jaundice. Azotemia was noted in 2 cases. Thrombophlebitis occurred in 2 cases, and was accompanied by a small pulmonary infarction in 1 of them. Vein ligation was not done in this case, and the episode did not recur. Three patients had residual pulmonary infection from an underlying atelectasis. Unexplained massive hemorrhage from the lower gastrointestinal tract occurred in a patient who had an extensive liver injury and moderate jaundice. No prothrombin determination could be done, and sigmoidoscopy and barium studies of the colon disclosed no abnormalities. Despite two episodes of bleeding, the patient steadily improved and was evacuated in good condition.

A discussion of the management of all these complications is not within the scope of this paper. Each was dealt with according to well established surgical principles. Maintenance of nutrition in certain patients presented considerable difficulty, however, and it is to a consideration of this problem that this report is directed.

### NUTRITIONAL STATUS AND PARENTERAL FLUID THERAPY

At the time of admission to this unit all 16 patients were suffering from varying degrees of anemia

\*From the Surgical Service of the 5th General Hospital, United States Army.

and acute malnutrition. Data on a representative number of cases are given in Table 2, which shows the amount of blood and plasma administered prior to arrival and the hemoglobin and serum protein levels on admission. It is evident that these patients would have benefited by a higher protein intake in the postoperative period prior to arrival.

Previous experience with abdominal wounds had convinced us of three facts — that profound anemia and nutritional edema develop with extraordinary

by vein precluded its use in these cases. Thus, when the caloric intake was low it became necessary to rely on small supplemental oral feedings, usually in the form of sweetened milk. These were often begun before all evidence of peritonitis or intra-peritoneal infection had subsided. Available vitamin preparations were given routinely as shown.

This regime effectively restored the levels of hemoglobin and serum protein to normal in all the patients in an average of seven to ten days. The re-

TABLE 1 *Nature and Extent of Injuries*

CASE No	CAUSE OF WOUND	NATURE OF ABDOMINAL INJURY	PART AFFECTED	ADDITIONAL INJURIES AND COMPLICATIONS
1	High-explosive shell	Perforating	Colon and buttocks	Compound fracture of sacrum
2	High-explosive shell	Penetrating	Colon and ileum	Wound of right thigh
3	Machine-gun bullets	Perforating (multiple)	Liver (multiple wounds)	Compound fracture of humerus
4	High-explosive shell	Perforating	Colon and ileum	Extensive wounds of abdominal wall
5	High-explosive shell	Perforating	Buttock, perineum and urethra	Compound fracture of radius
6	Rifle bullet	Penetrating	Duodenum and ileum	Extensive retroperitoneal hemorrhage
7	Rifle bullet	Penetrating	Right pleura diaphragm and liver	
8	Rifle bullet	Perforating	Jejunum, colon and liver	
9	High-explosive shell	Perforating (multiple)	Ileum (multiple wounds)	Extensive wound of buttock compound fracture of femur
10	Machine pistol bullet	Perforating	Left pleura diaphragm stomach colon spleen and pancreas	
11	High-explosive shell	Penetrating	Colon, rectum and bladder	Wound of buttock compound fracture of sacrum extensive retroperitoneal hemorrhage
12	High-explosive shell	Penetrating	Ileum jejunum and colon	Extensive wound of buttock compound fracture of sacrum
13	High-explosive shell	Penetrating	Ileum (multiple wounds)	Wound of buttock extensive retroperitoneal hemorrhage
14	High-explosive shell	Penetrating (multiple)	Ileum, jejunum and bladder	Extensive wound of buttock compound fracture of sacrum
15	Rifle bullet	Penetrating	Ileum (multiple wounds) and mesocolon	
16	High-explosive shell	Penetrating	Bladder and external iliac artery and vein	Extensive soft-tissue wounds compound fracture of pelvis

rapidity, that large amounts of protein are required to maintain a reasonable nutritional balance and that it is much better to prevent than to treat the nutritional disturbances that develop. To meet this problem a routine nutritional program for abdominal sepsis was adopted (Table 3). This regime is essentially the same as that recommended some years ago by Collier and Maddock<sup>4</sup> for salt and water balance, except that it substitutes 1 liter of protein-carrying fluid for 1 liter of 5 per cent dextrose and water. It provides approximately 50 gm of protein and 125 gm of carbohydrate daily. If there is a considerable loss of salt, the total carbohydrate intake may be as high as 200 to 300 gm. The daily parenteral caloric intake may thus vary between 800 and 2000, depending on the amount of glucose given. The well known impracticability of repeatedly giving concentrated solutions of glucose

sults of therapy in Cases 3 and 7 are shown in Figures 1 and 2, respectively. These are typical responses. The need for whole blood as well as plasma is illustrated in Case 7. In general, the more septic the patient was the slower was the response to therapy, but even in the sickest patients, whose cases are presented in detail below, the levels of hemoglobin and serum protein returned to normal within fourteen days.

The hazards of repeated large amounts of blood and plasma constitute an objection to this nutritional regime. In this series of 16 patients, fresh — one to seven days old — banked blood preserved in a sodium citrate-glucose mixture was used. Most of the blood was Type O. No serious transfusion reactions were encountered, and there was no evidence of massive hemolysis of either the patient's or the transfused blood. There were 7 cases in



which jaundice developed, but the available evidence indicated that severe sepsis rather than hemolysis was the principal contributory factor.<sup>8</sup> In 2 cases, moderate nitrogen retention without a true renal shutdown occurred. In one of these, the transfusions were continued and recovery ensued as soon as sepsis was controlled. In the other, death occurred from generalized toxemia and sepsis. Post

general nutritional status of the patients improved only when residual infection had been eradicated.

### THE ROLE OF INFECTION

The principal cause of the severe degrees of malnutrition encountered in these patients was infection. In every case in which residual abscesses were easily accessible and could be promptly drained,

TABLE 2 Previous Therapy and Laboratory Data on Admission

CASE NO	TIME OF ADMINISTRATION	PREVIOUS BLOOD AND PLASMA THERAPY		TIME INTERVAL days	LABORATORY DATA	
		AMOUNT OF BLOOD cc	AMOUNT OF PLASMA cc		HEMOGLOBIN %	TOTAL PROTEIN gm /100 cc
1	Preoperative	1000	500	16	71	5.1
	Postoperative	1000	500			
2	Preoperative	500	None	11	71	5.1
	Postoperative	4500	5000			
3	Preoperative	500	None	12	58	4.1
	Postoperative	None	500			
6	Preoperative	?	?	7	58	6.2
	Postoperative	1500	2000			
7	Preoperative	1000	1500	9	73	5.3
	Postoperative	None	None			
12	Preoperative	2000	2000	7	56	—
	Postoperative	1000	1000			
16	Preoperative	500	250	15	61	4.8
	Postoperative	1000	1000			

mortem the kidneys were grossly normal. Although histologically there was minimal evidence of so-called "hemoglobinuric nephrosis," the changes were not sufficient to be regarded as a significant contributory factor to death.

Although our experience with repeated transfusions of Type O whole blood and pooled dried plasma was uniformly satisfactory, there is in-

rapid convalescence resulted. In all cases in which there were deep seated peritoneal or retroperitoneal abscesses that could not be well localized or readily drained, convalescence was prolonged and progressive wasting of the subcutaneous tissues occurred. This was true even in patients who were able to take fairly large amounts of food by mouth. The degree of weight loss in some patients was ap-

TABLE 3 Guide to Daily Nutritional Requirements \*

REQUIREMENT	FORM GIVEN	AMOUNT	CALORIES
Basic salt	Physiologic saline solution	500 cc.	—
Basic water (to replace loss in urine and insensible fluid loss)	5 per cent glucose in distilled water	±2500 cc.	500 (125 gm. of carbohydrate)
Replacement for salt and fluid loss from gastric suction	5 per cent glucose in saline solution	Variable (volume for volume replacement of lost fluids)	Variable (200 per liter)
Ileostomy fistula and so forth			
Protein	Plasma and whole blood†	1000 cc	200 (>0 gm. of protein)
Vitamins	Vitamin B complex	50 mg	—
	Vitamin C (ascorbic acid)	100 mg (50 mg twice a day intramuscularly)	—
	Liver extract	1 cc. (intramuscularly)	—
	Vitamin K‡	10 mg	—

\*This regime is not presented as the ideal one. It was the one employed on the basis of the supplies available.

†All whole blood if hemoglobin level below 80 per cent.

‡Given if jaundice or intestinal fistula present.

creasing evidence that this therapy, especially if high-titer blood is used, produces hemolytic anemia.<sup>6</sup> Therefore, whenever possible, matched blood or type-specific plasma should be used. Indeed, albumin may eventually prove preferable to plasma for nutritional purposes.

In contrast to the prompt rise in hemoglobin and serum protein that occurred under this regime, the

palling, in several cases it amounted to over 60 pounds. It is therefore evident that the management of residual infection must be regarded as an essential feature of any nutritional program.

In dealing with infection, the following general principles were adopted. All localized, easily accessible abscesses were promptly drained. This was done even before the serum protein and hemo-

and acute malnutrition. Data on a representative number of cases are given in Table 2, which shows the amount of blood and plasma administered prior to arrival and the hemoglobin and serum protein levels on admission. It is evident that these patients would have benefited by a higher protein intake in the postoperative period prior to arrival.

Previous experience with abdominal wounds had convinced us of three facts — that profound anemia and nutritional edema develop with extraordinary

by vein precluded its use in these cases. Thus, when the caloric intake was low it became necessary to rely on small supplemental oral feedings, usually in the form of sweetened milk. These were often begun before all evidence of peritonitis or intra-peritoneal infection had subsided. Available vitamin preparations were given routinely as shown.

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10	Machine-pistol bullet	Perforating	Left pleura, diaphragm stomach colon spleen and pancreas	
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the chest, spleen, stomach, colon and pancreas. Post-mortem examination disclosed gross leakage from all the suture lines in the multiple wounds of the stomach and colon. The other death occurred as a consequence of long-standing intestinal obstruction associated with a large undrained retroperitoneal abscess. Although the intestinal obstruction was relieved by surgery after admission to this hospital, the patient gradually lost ground and

enterostomy through a right rectus incision, surrounded by gross infection. The midabdominal incision through which the original operation had been performed was grossly infected. Peritoneal or retroperitoneal infection was manifested by tenderness in the right lower quadrant and the lower abdomen. No definite abscess was apparent. The long wound in the right thigh involving the adductor muscles was moderately infected. There was a large sacral decubitus. The colostomy wound was clean, but the colostomy was not functioning.

Laboratory studies showed the serum protein to be 5 gm per 100 cc and the hemoglobin 61 per cent, despite moderate

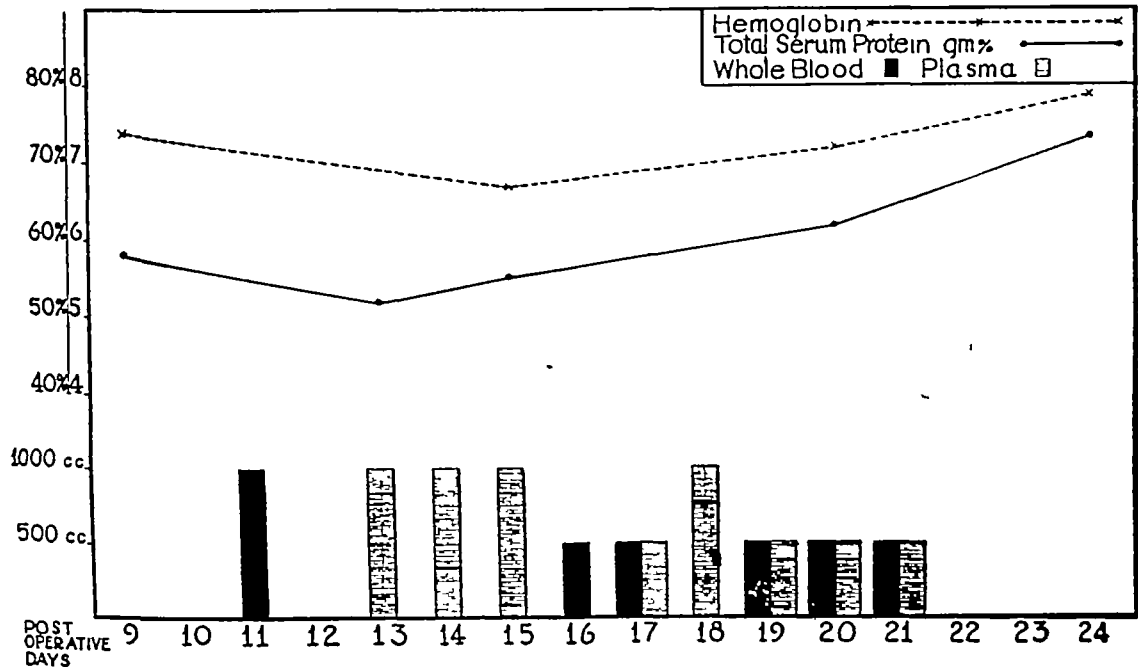


FIGURE 2

died of sepsis eight days later. The third case in this group is illustrative of this type of problem and is of sufficient interest to merit a detailed presentation.

**CASE 2** The patient was wounded on July 25, 1944, when a high-explosive shell fragment entered the anterior abdominal wall just to the right of the midline below the umbilicus. He was operated on 6 hours after injury at a field hospital under Pentothal Sodium anesthesia, and was found to have perforating wounds of the ileum and colon. A resection of the ileum, with end-to-end anastomosis, was done. The wound in the sigmoid was repaired with a purse-string suture, and a Mikulicz colostomy was performed proximal to the area of injury. A partial traumatic amputation of the left 5th finger was completed, and a wound of the right thigh was debrided.

The patient did well up to the 11th postoperative day, at which time he was given prostigmine. This was followed by signs of acute intestinal obstruction. On the following day, the abdomen was reopened and obstruction at the site of the anastomosis was found. A double-barreled enterostomy was done at the point of obstruction. Postoperatively the patient did poorly, although there was evidence of relief of the obstruction. He was transferred to this hospital on the fourth day after the second operation.

Physical examination on admission showed an acutely ill, extremely emaciated patient. There was slight jaundice and moderate peripheral edema. There was a double-barreled

dehydration. The patient had received sulfadiazine parenterally up to the time of admission.

Treatment consisted of daily infusions of blood or plasma, penicillin parenterally and frequent dressings to control infection and prevent digestion of the skin around the ileostomy. Although there was an ill-defined inflammatory mass in the right lower quadrant, the presence of the ileostomy, the profound nutritional disturbances and the patient's poor general condition rendered exploratory search too hazardous. The patient seemed improved one day and worse the next, and became progressively more jaundiced.

Despite supportive measures, the patient gradually lost ground, becoming irrational and semicomatose by the 15th hospital day. He showed evidence of nitrogen retention, the highest nonprotein nitrogen level being 84 mg per 100 cc, despite a parenteral fluid intake of 3000 to 4000 cc daily and a urinary output of 1500 to 2000 cc. The wound in the right thigh seemed to be developing a deep cellulitis. It was thought that this was due to retroperitoneal infection extending downward along the fascial planes and that the wound in the thigh might have continuity with the abdominal incision, but although the purulent discharge of the abdominal and thigh wounds was similar, actual continuity was never proved. The increase in drainage from the thigh coincided with an abrupt end of the downward course, and from this point on gradual improvement was noted. The icterus slowly cleared. Eventually further surgical drainage of the thigh was carried out. The spur on the double-barreled colostomy was cut down, and the wound infection cleared.

globin levels had been restored to normal. In the case of deep seated and poorly localized infection, a more conservative policy was adopted. It is well known that the peritoneum has a remarkable natural ability to deal with residual abscesses, accordingly, the patient was placed on the nutritional regime outlined in Table 2. Parenteral penicillin was given in amounts of 30,000 units every two hours, and the course of the disease was carefully observed. If the infection became well localized

removal was followed by a severe hemorrhage, which was finally controlled by packing. The abdomen was closed, the pack being left in the wound.

The patient was transferred to this unit on the 9th post operative day. He had a severe anemia and was profoundly septic, the daily temperature varying between 101 and 104°F. The packs were still in the wound, in which there was considerable deep infection, with marked digestion of the surrounding skin. There was mild jaundice. Examination of the abdomen revealed tenderness and a sense of resistance in the right upper quadrant on deep palpation that suggested a mass.

Initial therapy consisted of multiple plasma and whole blood transfusions, in accordance with the program outlined in Table 3. Removal of the pack in the wound produced no hemorrhage, but drainage became more profuse than ever, and at times appeared to be pure bile. Despite meticulous and frequent dressings, surgical drainage of the wound and the application of suction to the fistulous tract, the wound was slowly undermined by progressive infection. Although there was a gradual rise in the hemoglobin with multiple transfusions, the patient remained profoundly septic, and his general condition was obviously deteriorating.

On August 23, 24 days after the injury and 15 days after admission, the jaundice became intense. The patient refused all food by mouth and became markedly listless and apathetic. Part of this reaction may have been due to the disturbances of acid-base metabolism caused by the high intestinal fistula. Carbon dioxide determination could not be done, but there was no tetany, the urinary output was good, and the hemoglobin and serum protein levels continued to show an upward trend. The possibility that the multiple whole-blood transfusions had produced the jaundice was raised by some observers. The patient had had severe chills and sweats with the marked swings of temperature but none of these had been closely related to a whole-blood transfusion, and there had been no hemoglobinuria. There was bile in the urine. It was reasoned that there was an incompletely drained abscess in the right upper quadrant, that this partially accounted for the jaundice, and that the duodenal fistula would not heal or subside until it was drained. Until the duodenal drainage subsided the wound infection could not be expected to clear up.

Accordingly, on August 26, under local anesthesia, the right upper quadrant was explored through an oblique subcostal incision, the original wound, which was in the midline, being carefully avoided. In the right subhepatic space there was a huge cavity filled with the same type of fluid as that draining from the wound. It was impossible to demonstrate a communication with the original wound, but the exact limit of the cavity could not be felt. All fluid was removed, and the cavity was drained.

Following this operation there was steady improvement. The patient became more alert and resumed eating, and the jaundice began to diminish. It is interesting, however, that the temperature went higher than before, ranging between 101 and 105°F. Since the patient's general condition appeared improved the febrile reaction was disregarded, and at the end of 2 weeks the temperature began to decline. The fistula was diverted from the original badly infected abdominal wound to the oblique subcostal incision, and the original wound rapidly cleared up and healed. By vigorous efforts on the part of the nursing staff, the second wound was kept clean and in good condition despite the excessive amount of drainage, and it gradually healed, leaving only a small fistulous tract. Six weeks after operation the patient was ambulatory and afebrile. The wounds were healed, but there was still a small fistula, which on lipiodol injection was found to enter the second portion of the duodenum. It seemed likely that this would heal without further intervention.

The patient was evacuated in excellent condition. He made steady progress and was ready for return to duty 8 months after injury. The fistula healed spontaneously.

Patients with undrained areas of infection that cannot be readily localized present a still more baffling problem. There were 3 patients in this category, 2 of whom died. One death was due to rapidly progressive peritonitis. The patient had received extensive shell wounds of the left side of

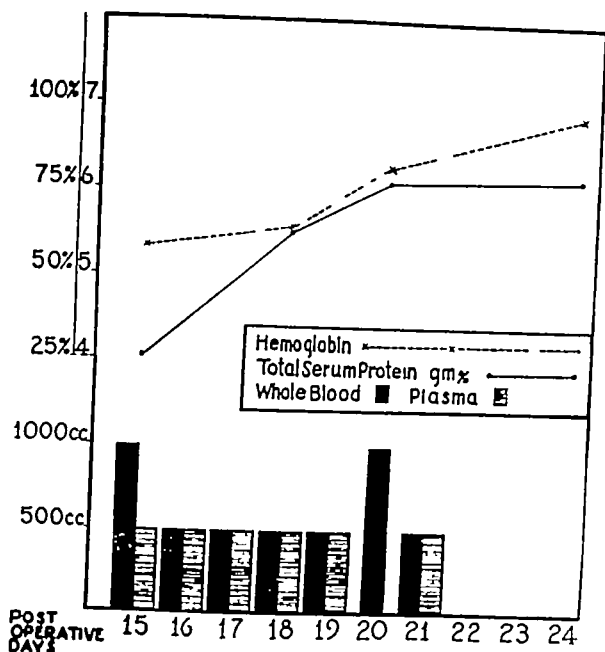


FIGURE 1

and easily accessible through "pointing," as in a pelvic abscess, it was drained. If no localization occurred but there was a gradual and steady improvement in the patient's condition, as evidenced by a rise in the hemoglobin and serum protein levels, a decline in temperature and an improvement in appetite, a conservative policy was continued. In 3 cases, complete resolution of intraperitoneal sepsis occurred under this regime and no surgical intervention was required. If, on the other hand, no improvement occurred or if the patient appeared to be losing ground, operation was carried out regardless of the risk it entailed, provided there was reasonably accurate localization of the infection by clinical signs. The following case report is illustrative.

**CASE 6** The patient received a perforating gunshot wound in the right upper quadrant of the abdomen on July 31, 1944. He was operated on 6 hours after injury and was found to have a perforation of the ileum, which was closed by suture. The bullet was felt in the retroperitoneal tissues in the region of the second portion of the duodenum. Its

considered under conservative therapy also made steady, although less dramatic, improvement. In these 12 cases the nutritional regime employed can be described as adequate. In 2 of the remaining 4 cases, convalescence was greatly prolonged by residual, poorly localized infection and by the presence of external intestinal fistulas. Under these circumstances, although anemia and hypoproteinemia were prevented, the patients steadily lost weight on the nutritional regime employed. As soon as infection was eradicated, however, they promptly improved.

Two patients died, one of overwhelming peritonitis shortly after admission and the other of inadequately drained retroperitoneal abscesses, which were not detected until the post-mortem examination. When it is considered that these cases were the most serious ones evacuated at the time from three different field hospitals, the end results may be described as gratifying.

#### DISCUSSION

In the postoperative care of the patient with war wounds of the abdomen, two cardinal principles should guide the surgeon — maintenance of nutrition and eradication of infection. These are complementary, since the well nourished patient can better resist infection and, conversely, nutrition improves as soon as infection subsides.

In actual practice, the maintenance of nutrition in these patients is difficult. Despite the liberal use of blood and plasma in forward areas, the enormous losses that may accompany extensive abdominal wounds are rarely completely replaced, and the nature of the injury in itself temporarily prohibits the taking of food by mouth. Thus, unless specific corrective measures are taken every patient develops a certain degree of anemia and malnutrition. Fortunately, if a good salt-and-water balance is maintained this period of starvation is readily withstood by the majority of patients, but if complications develop, particularly peritoneal or retroperitoneal infection, external fistulas and intestinal obstruction, the patient faces these additional burdens already seriously handicapped by malnutrition. Once a complication develops, the nutritional state deteriorates at an appalling rate.

It therefore becomes essential to attempt to maintain nutrition from the beginning by some such regime as that outlined in Table 3. The additional blood and plasma are little enough, and by no means satisfy the basic caloric requirement. A perfect parenteral food substitute has not been developed, but whatever substance is available should be employed to the fullest extent. The liberal use of blood and plasma in the early postoperative period is a step in the right direction. The administration of amino acids, — hydrolyzed casein, — either parenterally or in small amounts orally is desirable in the care of certain of these patients. Nutritional regimes

similar to those outlined by Co Tui et al.<sup>7</sup> and Elman<sup>8</sup> more closely meet the nutritional demands than does the regime employed in the present study. To the surgeon of the future it will seem as unwise to fail to feed these patients parenterally from the very moment of operation as it now seems to us to fail to transfuse a patient who has had a massive hemorrhage merely because he is likely to survive without transfusion.

The danger of residual infection demands constant vigilance. Adequate drainage of wounds and of local and easily accessible abscesses must be carried out promptly. In the case of deep-seated peritoneal and retroperitoneal infection, the condition of the patient must be weighed in the balance. If he is obviously getting well, the problem may solve itself. The natural ability of the peritoneum to combat residual infection is well known and is confirmed by this study. It is in the patient who is not getting well that an aggressive attitude toward residual infection must be adopted. Subphrenic and pelvic abscesses may be diagnosed with relative ease, and their management is standardized. Foreign bodies should be regarded as a possible clue to the location of obscure infection. If these sources are excluded, it is our conviction that in the failing patient an exploratory search for hidden abscesses is justified. This may indeed appear a drastic measure, and sound judgment must be exercised in appraising the given patient, but by this means certain lives can be saved that would otherwise be lost.

Since the presence of external fistulas adds a serious burden to the patient convalescing from abdominal wounds, open ileostomies should be avoided. Associated infection, however, appears to have a more deleterious effect on the nutrition of a patient than does external fistula alone. If infection can be controlled, a fistula may heal spontaneously. If a patient is losing ground, surgical repair of a fistula should not be delayed.

#### SUMMARY

A report is presented of the nutritional problems encountered in a series of 16 patients with extensive abdominal wounds. The series was a selected one in that these patients were too ill to be evacuated directly to the United Kingdom during the early weeks of the campaign in Normandy.

The need for an adequate nutritional regime in the early postoperative care of these patients is emphasized. The liberal use of blood and plasma, not only before but for some time after operation, is necessary.

A routine nutritional program is presented. In cases in which residual infection was readily eradicated this program proved adequate. When there was persistent infection, convalescence was prolonged and a parenteral food substitute to increase the total caloric intake would have been desirable.

The patient soon began to take food by mouth, and from this time on his progress was steady. The jaundice cleared entirely, the azotemia subsided, and the blood picture returned nearly to normal. On October 4, an attempt was made to cover the large sacral ulcer with skin. Although the granulations appeared healthy, a split-thickness graft failed to take. On October 18, an attempt was made to close the ileostomy under local anesthesia. No attempt was made to free the bowel because it seemed that the patient's general condition would not withstand an extensive procedure, but the closure broke down 36 hours after operation. Despite the leaking ileostomy he continued to improve, and he was evacuated in fair condition. Subsequent reports indicate that he made a slow but steady recovery.

The management of this type of case remains a problem, but it is our belief that if improvement does not occur under so-called "conservative" management, an operation to find and drain the infection must be undertaken even if it requires an exploratory laparotomy. In this case a more aggressive policy, with drainage of the peritoneal infection and closure of the ileostomy at an early date, might have been wiser. If spontaneous drainage of the retroperitoneal infection had not occurred, the patient would probably not have recovered. In this type of case, in which convalescence is prolonged by deep-seated, poorly localized infection, the maintenance of nutrition is exceedingly difficult. It is comparatively easy to prevent hypoproteinemia and anemia by frequent transfusions of blood and plasma, but despite this fact there is progressive weight loss and wasting of the subcutaneous tissues. Small amounts of highly nutritious liquids may be given by mouth, but at times these are not well tolerated, and even when they are it is difficult to raise the caloric intake above 2500 daily. Under such circumstances the use of protein digests, which were not available, would be desirable.<sup>7, 8</sup>

#### EXTERNAL FISTULAS

There were 5 patients with external fistulas, — in the urinary tract in 3 cases, in the duodenum in 1, and in the ileum in 1. The urinary fistulas were relatively innocuous so long as there was adequate external drainage. The 2 patients with intestinal fistulas, whose cases have been presented in detail, presented extremely serious problems. It is significant, however, that once infection was controlled their general condition improved despite the presence of the fistula, and in 1 case the fistula healed spontaneously. The difficulties encountered in the case in which an ileostomy had been performed support the contention of the surgeons who maintain that ileostomies cause more deaths than cures. Also, it is evident that if a patient is losing ground, a surgical attack on the fistula should be undertaken early, before his condition has deteriorated to such a point that even a limited procedure cannot be tolerated.

#### CHEMOTHERAPY

All these patients had received sulfanilamide in the wound and sulfadiazine and penicillin paren-

terally prior to admission to this hospital. There was considerable variance in the dosages used and, so far as could be determined from the records, some irregularities in the schedule of administration. In general, however, all the patients had received combined therapy in reasonably adequate dosages over periods of seven to sixteen days. On arrival at this hospital the sulfonamides were discontinued. This was done for several reasons. First, it was argued that whatever residual infection these patients showed had developed despite the use of the drugs, and that therefore their continued use was not likely to be beneficial. Second, the probable nature of the infection — namely, a localized collection of undrained pus — made it unlikely that sulfonamide therapy would affect it. Third, the continued use of sulfonamide drugs, with their tendency to produce toxic and febrile reactions, would add an additional factor to cases already so complex that interpretation of the cause of fever was difficult. Finally, and most important, it seemed unwise to continue the use of these drugs in patients with such profound metabolic disturbances — that is, dehydration, anemia, hypoproteinemia, azotemia and jaundice.

The sulfonamide drugs were discontinued because of certain specific objections to their use. Since no such objections were known to pertain to the use of penicillin, and since it seemed unwise to discontinue all chemotherapy, this agent was employed routinely in large amounts — 30,000 units every two hours. We were influenced in this decision by two things. First, the controlled observations of Lyons<sup>9</sup> indicate that the nutritional status of patients with septic wounds is restored to normal more rapidly when penicillin is given, as well as blood and plasma. Second, our previous experiences with the use of this drug had revealed dramatic improvement after its use in several patients gravely ill with longstanding abdominal sepsis.

Since penicillin was used routinely without control periods of observation, there are no data on which to base an appraisal of its value. Although it was given in large amounts over a period of many days and weeks, — one patient received 4,000,000 units, — no toxic reaction was observed. The repeated hypodermic injections became an ordeal for some patients, particularly those whose convalescence was prolonged. It is our impression, based only on a comparison between the course of these cases and our recollection of the course of similar cases treated without penicillin, that the drug was of value.

#### RESULTS

The nutritional state of 9 of the 16 patients rapidly improved under the regime outlined in Table 2. These were the patients in whom sepsis was promptly eradicated by adequate drainage. Three patients in whom residual peritoneal infection sub-

blood pressure of the upper extremities of dogs in which experimental coarctation was induced by means of Goldblatt clamps applied to the aorta. He attributes this phenomenon to the prompt and ready development of collateral channels in these animals.

King<sup>10</sup> has pointed out that with embarrassment of circulatory compensation the blood pressure may drop to normal levels, and he has in addition reported a case in which a normal tension in the brachial arteries was found in an asymptomatic woman, in whom he postulated the existence of an aortic coarctation. The patient presented physical evidences of collateral circulation and a blood pressure lower in the popliteal arteries than in the brachials, with dilatation of the ascending aorta the only striking radiologic feature.

Failure to palpate both radial pulsations simultaneously or to determine blood pressure as a routine in the right arm, when only unilateral readings are taken, obscures the presence of a hypertension or pulse asymmetry in cases in which the pathologic process extends to or above the origin of the left subclavian artery.<sup>11,12</sup> That the right arm rather than the left should be chosen for routine unilateral blood pressure determinations is a point that has been insufficiently stressed. King<sup>10</sup> has emphasized the work of Korms and Guinard and of Stueglitz and Propst, who have pointed out that in most persons the blood pressure in the right arm is usually higher than that in the left. The reasons given for this difference have been many, but the difference in the anatomy of the blood supply to the right and the left upper extremity is probably the most important single factor.

As pointed out by Gitlow and Sommer,<sup>13</sup> in cases in which the collateral circulation is well established and constant, no difference in pulse volume and blood pressure between the upper and lower extremities may be detectable by ordinary clinical means. One of the patients of Stewart and Bailey<sup>14</sup> showed no reduction in the blood pressure of the legs as compared with that of the arms.

The third diagnostic criterion — namely, the presence of a loud systolic murmur over the manubrium and in the left interscapular space — is of importance only in indicating the need for an extension of the search for its etiology. Nothing is pathognomonic about the murmur, since its character varies in different cases.

Pulsation of the subscapular, intercostal and internal mammary arteries, interpreted as evidence of marked development of collateral circulation, is considered one of the most valuable clues to the diagnosis of coarctation of the aorta. Although such conditions as aneurysm, intrathoracic neoplasm and certain types of exophthalmic goiter may, as pointed out by Blackford,<sup>2</sup> produce a similar finding the possibility of confusion is not great. Indeed, King<sup>10</sup> believes that the evidence of collateral arterial

circulation is the most important single clue to the diagnosis, this sign having been present in all the 16 cases of coarctation that he has examined. In Blackford's series, collateral circulation was clinically detectable in 35 cases, was not mentioned in 15 cases, although it was implied in about half of these, and was absent in 5 cases. In one of the cases reviewed, the patient, a pilot, who while living presented no clinical evidence of superficial collateral circulation, was revealed at post mortem to have had dilated internal mammary vessels serving as the principal site of the necessary shunt.

It is apparent that the clinical detection of evidences of collateral circulation depends in great degree on which of two main routes of blood flow is utilized.<sup>15</sup> If there is anastomosis of the branches of the subclavian artery, such as the superior intercostal, postscapular, interscapular and subscapular arteries, together with the aortic branches of the internal mammary arteries, with the first four intercostal arteries, most of the blood thus being carried into the descending aorta and thence to the lower extremities, the evidences of collateral circulation may well be marked. If, however, a more circuitous but less superficial anastomosis — that of the internal mammary arteries with the superior and inferior epigastric arteries — occurs, clinical evidence of collateral circulation may not be so obvious. It is in the latter instance especially that a useful diagnostic procedure — namely, simultaneous palpation of the right radial and femoral pulses — is a valuable adjunct, in that a distinct lag in the summit of the femoral pulse may be felt. As a corollary, it can be stated that a diminished or absent femoral pulse<sup>15</sup> was noted in many of the cases reported.

The latter finding unfortunately has assumed undue prominence in the diagnostic armamentarium of many clinicians, and it is with this phase of the subject that the present paper is primarily concerned. It has been our experience that many physicians in examining cases in which coarctation of the aorta must be considered in the differential diagnosis have ruled out its presence on finding normal femoral pulsations, or pulsations in the more peripheral arteries of the lower extremities. This misconception has crept into the literature. In Musser's<sup>16</sup> textbook it is stated, "The blood pressure reading from the arms is usually elevated, whereas the pulsation in the femoral arteries is greatly reduced or may even be imperceptible." In a recent article, Baker<sup>17</sup> states that a cardinal sign of coarctation of the aorta is absence of pulsations in the peripheral arteries of the lower extremities. "If a feeble pulsation is detected over the femorals," he continues, "it is asynchronous with the radial pulse. If the pulsations of the dorsalis pedis and posterior tibial arteries are present, coarctation can be excluded as a possibility without further ado." In a paper by Green<sup>18</sup> it is stated to be the practice to palpate routinely for pulsations in the femoral arteries. If

The management of residual or latent infection is an essential feature of any nutritional program. Adequate drainage of wounds and of localized abscesses must be promptly performed. A persistent search for undrained foci of infection must be carried out, and on occasion in the failing patient an exploratory operation is justified.

Since external fistulas add a serious burden to the patient with abdominal wounds, open ileostomies should be avoided. Associated infection, however, appears to have a more deleterious effect on the nutrition of a patient than does an external fistula

alone. If infection can be controlled, a fistula may heal spontaneously.

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## COARCTATION OF THE AORTA\*

### A Report of Two Cases

MAJOR ROBERT FRIEDENBERG, M C, A U S, AND CAPTAIN ARCHER J. SOKOL, M C, A U S

SINCE the first case of coarctation of the aorta was recorded in 1791, many excellent papers concerning the nature of this interesting condition have been published. Both the infantile and adult forms, with their pathogenesis, anatomy, associated diseases, such as cerebral and other types of aneurysms, symptomatology and diagnostic and constitutional characteristics have already been ably and exhaustively reviewed.<sup>1-5</sup> Indeed, Lewis<sup>4</sup> states, "So much has been written about coarctation of the aorta that new records of cases can have little value unless they reveal new features of interest or importance to the study of the condition." This statement might well dissuade one from writing another paper on the subject, were it not for the need of calling attention to some of the uncritical diagnostic procedures that have won general usage. For example, many physicians, with a false sense of assurance, rule out the presence of coarctation of the aorta by the finding of a normal femoral pulse. A review of the literature and study of the 2 cases presented in this paper indicate that diminution or absence of the femoral pulsation in aortic coarctation is one of the less constant signs.

According to Pardee,<sup>6</sup> the major criteria in this anomaly are four in number. They are as follows: erosions of the margins of the ribs, absence of the aortic knob and dilatation of the ascending aorta, a high blood pressure limited to the upper extremities, a loud systolic murmur audible over the manubrium sterni and in the left interscapular area, and pulsations of the subscapular, intercostal and internal mammary arteries.

Even a cursory review of the literature reveals that almost any of these features may be absent or

obscure in a given case. Thus, absence of rib crenations, especially in younger patients, is not unusual. Lack of prominence rather than absence of the aortic knob in the radiographic silhouette is frequently seen in coarctation of the aorta as well as in other types of cardiac disease. In left-oblique films, the retroaortic and retrocardiac spaces are said to be clear in cases of coarctation,<sup>7</sup> instead of presenting the normal haziness in this area ordinarily produced by the ascending arch and the upper portions of the descending thoracic aorta. These findings may, however, be obscured, since young persons may normally show minimal density of the aortic shadow.

Left-ventricular hypertrophy is not a regular finding, and its presence in so many other cardiovascular diseases limits its value as a pathognomonic sign in this one.

Dilatation of the ascending aorta seems to be the most constant radiologic feature, excluding, of course, angiocardigraphic studies, which at present are not in widespread use. Syphilitic aortitis may produce a similar picture, but the differentiation should not prove difficult. Thus, it is seen that in ordinary radiographic or fluoroscopic examination the combination of dilatation of the ascending aorta and lack of prominence of the aortic knob is the most frequently demonstrable finding.

A high blood pressure limited to the upper extremities is one of the most constant features of the disease. The reason for the hypertension has not been unequivocally demonstrated. The theory most favored postulates an increased peripheral resistance by the coarctation and the collateral circulation as the main cause.<sup>8</sup> Page,<sup>9</sup> however, has been unable to demonstrate a consistent rise in the



Posteriorly systolic bruits were heard over the left chest. No visible palpable arterial pulsations were noted posteriorly.

Fluoroscopic examination in the posteroanterior position revealed elongation and rounding of the left lower ventricular contour, with an undulating type of pulsation at the waist of the heart. The ascending aorta was broadened, pulsations were moderately exaggerated, and the aortic knob was not so prominent as it normally is. In the right anterior oblique position, there was moderate encroachment on the retrosternal space. The width of the aorta at its uppermost margin seemed normal. In the left anterior oblique position, there was a markedly expansile type of pulsation in the region of the outflow tract of the left ventricle. The contour of this portion of the left ventricle seemed more convex than that normally seen. The ascending aorta appeared broader and more anterior in position than normal. The aorta could not be traced under the arch. X-ray examination of the chest revealed areas of cretation along the lower borders of several of the ribs. The diagnosis was coarctation of the aorta, with an enlarged heart.

The electrocardiogram revealed a rate of 78, with a sinus rhythm. A small Q<sub>1</sub> and inverted T<sub>3</sub> were present. There was a tendency to left-axis shift.

The patient in Case 1, aside from presenting what was suggestive of a subsiding infectious mononucleosis, was admitted with a dispensary diagnosis of pleurisy. Analysis of his symptoms showed that the chest pain was undoubtedly related to coarctation of the aorta. The pain was in all probability due to root or nerve pressure caused by passage of the enlarged anastomotic arteries through the intervertebral foramina.<sup>2,3</sup> The patient sustained an injury of the left foot and leg from a hand grenade, and ten hours later operation was performed for arterial repair in the left thigh and repair of an artery above and posterior to the ankle. According to the patient, recurrence of bleeding at the site of the arterial repair in the thigh ten days later necessitated reoperation. This injury may explain the absence of the dorsalis pedis and posterior tibial pulsations in the left foot contrasted with the right.

Case 2 is that of an asymptomatic medical student who had previously been repeatedly examined during participation in the Army Specialized Training Program. Hypertension, which was brought down to the upper limits of normally accepted standards by rest, was known to be present. Apparently the absence of visible and palpable evidences of collateral circulation, as well as the presence of a normal femoral pulse, had previously diverted the minds of the examiners from the possibility of aortic coarctation.

The autopsy incidence of coarctation of the aorta is said to be 1/1550.<sup>3</sup> To increase the accuracy of an intra-vitam diagnosis, primary stress must be placed on the most constant diagnostic features, as a preliminary screening measure in ruling out the presence of aortic coarctation. That there is no one clinically detectable and universally constant feature that is easily demonstrable in the course of a routine examination has been shown. Even the almost universal finding of a blood pressure higher in the upper extremities than in the lower was absent in one of the cases reported by Stewart and Bailey.<sup>14</sup> Except, however, for angiocardigraphic studies

such as those made by Grishman et al.,<sup>12</sup> which do not lend themselves to widespread usage, this decrement in arterial pressure in the legs as compared with that in the upper extremities seems to us, as well as to Stewart and Bailey,<sup>14</sup> the most frequent and readily detectable distinctive feature of coarctation of the aorta. The determination of the blood pressure in the lower extremities, although possibly irksome to the busy practitioner, must be made in every case in which otherwise unexplained factors exist, such as bizarre types of murmurs or bruits heard anywhere in the chest, arterial hypertension or prominent or unusual arterial pulsations, regardless of the age of the patient.

At present, the value of prompt diagnosis, aside from the desire for scientific accuracy, lies in the advantage of guiding patients intelligently in forming patterns of activity and hygiene within the limits of their vasculature. Possibly, the future holds promise for more active surgical therapy.<sup>24</sup>

## SUMMARY

The major criteria for the diagnosis of coarctation of the aorta are reviewed and evaluated, and 2 cases are described.

A brachial blood pressure higher than the popliteal blood pressure is one of the most constant and easily detectable clinical features of the disease.

Delayed, diminished or absent femoral pulsation may be noted in many cases but this sign cannot be relied on routinely to rule out coarctation of the aorta.

Determination of the blood pressure in the lower extremities must be made in every case in which otherwise unexplained factors exist, regardless of the age of the patient.

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these are absent, the blood pressures are taken. Others<sup>19, 20</sup> have also recommended palpation for femoral pulses as a necessary procedure. This practice is in conflict not only with our experience but also with that of others. Thus, Stewart and Bailey<sup>14</sup> discovered in their series of cases that the absence of pulsations in the arteries of the legs was an inconstant finding, not only in the femoral vessels but in the popliteal and dorsalis pedis as well.

Certainly, a sign more constant than pulse changes in the lower extremities should be relied on in routinely ruling out coarctation of the aorta. Many other writers have called attention to the basic inadequacies of femoral palpation as an absolute diagnostic criterion. Abbott<sup>1</sup> in her encyclopedic review points out that retardation and diminution or even absence of the femoral pulse is not constant, either in its presence or in the extent of diminution. Blumgart, Lawrence and Ernstene<sup>8</sup> have made a similar statement. One of their patients showed pulse waves in the femoral arteries approximately equal to those in the radials, and the radial pulse wave appeared approximately 0.05 seconds before the femoral. Differences of this small degree are not detectable by the usual gross clinical methods of palpation. Furthermore, in the case cited the popliteal and dorsalis pedis pulsations were perceptible but weak, although the posterior tibial pulses were not felt. Considering the facts that the patient was sixty-six years old and that auricular fibrillation was present as well, it becomes evident that overattention to the pulse in the lower extremities without due regard to the other more significant signs may cause one to miss the diagnosis. In pulse tracings taken by Railsbach and Dock<sup>21</sup> in a case of coarctation of the aorta, the femoral arterial pulse followed the radial by 0.02 seconds, a time lag certainly within the limits of subjective error of the observer.

In short, we agree with such writers as Goodson<sup>22</sup> that a retarded, diminished or absent pulse in the lower extremities in the presence of a full, bounding pulse in the upper extremities is pathognomonic of coarctation of the aorta provided embolism in the iliac arteries is ruled out. But this statement is accepted in the sense that this finding is pathognomonic only when present, and that coarctation not infrequently exists in its absence.

There follow the reports of 2 cases in which the femoral pulsations were easily palpable and of normal volume, with nothing in the nature of the pulsations that was considered as diagnostically significant.

### CASE REPORTS

**CASE 1** The patient, a 25-year-old German prisoner of war, entered a station hospital on June 28, 1944, complaining of sore throat and pain in the left side of the back over the lower ribs of 10 days' duration. He was a well developed and well nourished, broad-shouldered and narrow-waisted man of athletic build. There had been no unusual childhood

diseases. The patient had experienced some dyspnea on moderately severe exertion for the last 3 years, especially when swimming. For the last few years he had noted pains in the left side whenever he engaged in unusually strenuous work or exercise. The pains were stabbing, were aggravated by movement and by bending and usually disappeared spontaneously after 5 or 10 minutes' rest. On January 30, 1944, this patient's left foot and leg were injured by the explosion of a hand grenade. He was operated on 10 hours after injury for repair of the posterior tibial artery (?) of the left leg and also for arterial repair in the medial aspect of the left thigh above the knee. Because of recurrence of bleeding a second operation was performed 10 days later.

Early in the following June, the patient was sent to pick onions on a farm, and shortly thereafter the pain in the back became more constant, with fewer intervals of freedom from pain. It was especially aggravated by bending forward. It was localized over the left lower ribs and was neither severe nor completely disabling.

Physical examination revealed traumatic and operative scars at the medial aspect of the lower third of the left thigh and the lower third of the left leg over the posterolateral area. The pharynx was slightly injected. Forceful carotid pulsations were noted in the neck, and a systolic bruit was present. Systolic bruits were heard best over both infraclavicular fossas and at the level of the 3rd rib posteriorly in the inter-scapular area. There was a visible pulsatile and palpable artery, somewhat tortuous in its course, over the medial and upper border of the right scapula. An occasional sibilant rale was heard posteriorly. Vascular examination revealed a posterior tibial artery pulse barely palpable on the right and nonpalpable on the left, and a dorsalis pedis pulse weakly palpable on the right and absent on the left. The femoral pulses were easily palpable and of normal volume bilaterally. The radial vessels were somewhat thickened in relation to the patient's chronologic age. The blood pressure was 180/100 in both arms and 120/100 in both legs.

Cardiac examination revealed visible arterial pulsations over the left anterior axillary area. There was accentuation of the aortic second sound, with palpable closure of the aortic valve and a blowing systolic aortic murmur. A musical systolic murmur, moderate in duration, was heard at the apical region and was transmitted to the left anterior axillary region, and also to the right toward the xiphoid process and along the left sternal border. The rhythm was regular, and there was no displacement of the apex or increased manubrial dullness. The spleen was palpable, firm and nontender and was felt 1 fingerbreadth below the left costal margin. Pulsations of the abdominal aorta were not felt.

The red-cell count was 4,370,000, and the hemoglobin 13.5 gm. The white-cell count was 5400, with 55 per cent neutrophils, 33 per cent lymphocytes, 9 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. Urinalysis, a Kahn test and a blood smear for malarial organisms were negative. The sedimentation rate was 11 mm in 60 minutes. The heterophil antibody test revealed agglutination in a dilution of 1:112.

X-ray examination of the chest in different projections revealed widening of the base of the heart and the ascending portion of the aortic shadow. Fluoroscopic examination showed a strong impulse on the right side of the cardiac shadow and absence of a true aortic arch. Irregular crenation defects were present along the inferior margins of many of the ribs posteriorly. The bronchovascular markings were prominent, but the pulmonary structures were essentially normal. The findings described were compatible with a coarctation of the aorta. The electrocardiogram revealed a normal axis with small Q waves in Leads 1 and 2, a large Q wave in CF, and a diphasic T.

**CASE 2** The patient, a well developed, 22-year-old medical student, had known of the existence of hypertension for some time. Previous examinations had always revealed an initial elevated tension, which was brought down to almost normal limits by rest. The past history was noncontributory.

The blood pressure was 174/100 in the right arm and 180/100 in the left in the supine position. Femoral pulsations were readily palpable and of normal amplitude. The blood pressure in the right leg was 120/95. In the supine position there was a blowing systolic bruit, heard best over the xiphoid and transmitted to the left. There was also a blowing systolic pulmonic murmur of moderate duration and intensity. In the erect position there was heard an impure first apical sound.

TABLE 1 Data in Patients with Known Precursors to Diabetes

Case No.	Age	RELATIVES WITH DIABETES	HEIGHT	NORMAL WEIGHT	DATE OF ONSET	DATE OF HOSPITALIZATION	REGIME ON DISCHARGE	HISTORY OF ONSET
1	22	0	5 ft 8 in	180	Apr 1944	Oct 1944	C200-P80-F80 PZI 15 units RI 10 units.	Gradual onset in England of polyuria, polydipsia and polyphagia with 40 pounds weight loss
2	25	Brother	5 ft 5 in	172	Nov., 1944	Dec 1944	Regular diet	Gradual onset of polyuria while overseas; patient developed laryngitis, and routine urine examination revealed sugar
3	33	Mother	5 ft 5 in	195	?	Oct 1944	Regular diet	Routine urine examination revealed sugar during hospitalization overseas for upper respiratory infection
4	27	0	6 ft	192	Aug 1944	Aug 1944	C250-P80-F80 PZI 10 units	Gradual onset of polyuria and polydipsia while overseas
5	29	0	5 ft 7 1/4 in	185	June 1944	?	C160-P100-F80 PZI 10 units	Gradual onset of polyuria and polydipsia with development of mild acidosis
6	27	Father maternal aunt	5 ft 8 in	205	?	?	C150-P80-F70 PZI 10 units	Routine urine examination revealed sugar on admission to overseas hospital for circumcision
7	38	Mother	5 ft 9 1/2 in	225	May 1942	Oct 1944	C110-P75-F40	Routine urine examination revealed sugar during hospitalization for gall bladder disturbance prior to going overseas
8	44	0	5 ft 10 in	200	Oct. 1943	Mar 1944	C200-P90-F100	Routine urine examination revealed sugar
9	21	Paternal uncle	5 ft 6 1/2 in	166	Mar., 1944	Mar 1944	C150-P90-F80 PZI 26 units	Polyuria, polydipsia and acidosis developed after several weeks of combat duty including continuous exposure to artillery fire
10	19	Maternal grandmother	6 ft 1 1/2 in	170	Sept 1944	Oct 1944	C250-P85-F110 PZI 35 units.	Gradual onset of polyuria and polydipsia and loss of 20 to 30 pounds in weight while overseas
11	43	0	5 ft 6 in	223	?	Sept 1944	Regular diet	Based on glucose-tolerance test patient asymptomatic but had cirrhosis of liver
12	24	Maternal grandmother	5 ft 7 in	190	Dec 1944	Jan 1945	C200-P80-F90 PZI 17 units	Onset of symptoms after considerable stress and strain while in an infantry unit in active combat
13	21	0	5 ft 9 in.	180	Dec 1944	Jan 1945	C250-P100-F100	Gradual onset of polyuria while overseas
14	35	Mother	5 ft., 8 in	212	1941	Feb. 1945	C200-P80-F90	Disease existed prior to service; diabetes rediscovered three years later when sulphur dermatitis proved refractory to treatment and urine examination revealed glycosuria
15	36	0	5 ft 8 1/2 in	200	1942	Feb 1945	C200-P75-F70 PZI 25 units	Migraine headaches for years followed by gradual onset of polyuria and loss of weight; glycosuria found on routine admission for migraine.
16	40	Brother	5 ft 3 3/4 in.	232	1941	Jan 1945	C130-P65-F40	Onset prior to service, when patient had a carbuncle of neck and was treated with diet and small doses of insulin; a recurrence of polyuria Jan 1945 while overseas.
17	43	0	5 ft. 8 1/2 in	154	?	May 1945	Regular diet	Routine urine examination revealed sugar while awaiting separation from service
18	30	0	5 ft 11 in.	215	Apr., 1945	May 1945	PZI 10 units, RI 3 units	Gradual onset of polyuria and polydipsia after dissatisfaction with job on return from overseas
19	28	Sister (died in coma)	5 ft 6 in	147	Mar., 1945	Apr 1945	C190-P65-F100 PZI 40 units RI 15 units	Polyuria and nocturia hospitalized for influenza, given penicillin treatment for latent syphilis 1 wk. later admitted with vomiting and glycosuria and acetoneuria found
20	22	Maternal grandmother	5 ft 4 3/4 in	150	Dec. 1944	Apr 1945	C200-P80-F100	Polyuria and increased thirst while on duty overseas
21	43	0	5 ft., 8 in.	228	1938	Mar 1945	Regular diet	Diagnosis made at Walter Reed Hospital in 1938
22	54	0	6 ft. 1 1/2 in	190	June, 1944	Jul. 1944	C200-P85-F100	Polydipsia nocturia loss of weight and ulcer of foot while overseas
23	37	0	5 ft 9 in	214	?	Nov., 1944	C150-P75-F75	Dermatitis following administration of benzyl benzoate for scabies; routine urine examination revealed glycosuria
24	38	0	5 ft 8 1/8 in	175	May 1944	Apr 1945	C200-P90-F100 PZI 30 units	Polyuria and nocturia while overseas
25	49	0	5 ft. 6 in	180	1943	June, 1945	C175-P80-F90	Some increase in thirst and slight polyuria after entry into the service; routine urine examination revealed glycosuria at a separation center

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## PSYCHOGENIC FACTORS IN THE ETIOLOGY OF DIABETES

MAJOR B R GENDEL, M C, A U S, \* AND COLONEL JULIEN E BENJAMIN, M C, A U S †

EVER since the demonstration by Von Mering and Minkowski that extirpation of the pancreas in dogs produces diabetes, a great deal of research work has been performed to elucidate the pathogenesis of this disease. The influence of heredity has been stressed, and the evidence that diabetes is inherited as a Mendelian recessive has been presented by Pincus and White.<sup>1</sup> Additional factors, such as obesity, have also been evaluated. From the experimental field, the relation of diabetes to the pituitary gland has been demonstrated by Houssay<sup>2</sup> and that to the adrenal glands by Long and Lukens.<sup>3</sup> Recently, the study of experimentally induced alloxan diabetes<sup>4</sup> has opened new possibilities for research. Fundamentally, however, the factors that operate to precipitate diabetes are not clear, nor is the mechanism whereby these factors operate.

Transient glycosurias following emotional disturbances have been described. Boehm and Hoffmann<sup>5</sup> produced glycosuria in cats following the arousal of rage and the application of painful stimuli. Cannon, Shohl and Wright<sup>6</sup> reproduced these experiments without the use of painful stimuli. Folin, Denis and Smillie<sup>7</sup> reported that 18 per cent of 34 second-year medical students and 17 per cent of 36 female college students showed traces of sugar in the urine immediately following an examination. Glycosuria produced in this manner has been called "emotional glycosuria." It has not been shown to become permanent, nor has diabetes ever been produced experimentally in this manner.

A review of the literature concerning the possibility of producing diabetes by psychic trauma reveals some interesting differences of opinion. Clinicians with great experience in treating diabetics, such as Joslin,<sup>8</sup> Root<sup>9</sup> and Von Noorden,<sup>10</sup> are not convinced that such a relation of cause and effect exists. Joslin cites Von Noorden's experience in World War I to the effect that neurogenic diabetes does not occur. As a consultant for a hospital center in France through which 40,000 soldiers passed, Joslin discovered only 2 cases of diabetes, despite his known interest in this particular disease. Matz<sup>11</sup>

studied diabetes in veterans of World War I, and came to the conclusion that neurogenic factors are of no importance in the etiology of diabetes.

On the other hand, investigators in the psychiatric field, particularly Menninger<sup>12</sup> and Daniels,<sup>13</sup> are not so convinced that the subject is closed. They believe not only that there is a correlation between mental stress and strain and increases in the severity of the diabetic state but that diabetes may be initiated by psychologic or emotional disturbances. Our interest in this phase of the problem arose after observing several patients in whom a psychogenic trauma seemed to precede the development of diabetes in such a way as to suggest cause and effect.

The records of all patients who were treated for diabetes on the Medical Service of the Lovell General Hospital between August 1, 1944, and June 30, 1945, — a total of 44 cases in 21,993 admissions, — were reviewed. All these patients were seen personally by us.

The diagnosis of diabetes mellitus in these patients was based on either one of two criteria. The first of these was the occurrence of an illness characterized by hyperglycemia — with a blood-sugar level of 300 mg per 100 cc or more — associated with glycosuria and occasionally with acetonuria, and necessitating a diet and moderate to large doses of insulin — 30 or more units daily — for complete control. Some of the patients had had glucose-tolerance tests done overseas and typical diabetic curves had been obtained. In others, no such test had been made, but when an attempt was made to reduce the dosage of insulin, glycosuria and hypercemia appeared, although the patient was on a strict diet and was taking 30 or more units of insulin a day. It was not considered either necessary or desirable to perform a glucose-tolerance test in these cases. The second criterion was as follows. In mild cases of glycosuria, glucose-tolerance tests were done, and in many cases these were repeated after the patients had been on a high-carbohydrate diet for about a week, especially if there was any doubt about the original diet. The diagnosis of diabetes mellitus was made if the blood-sugar value in the test exceeded 180 mg per 100 cc at its peak and did not return to normal within two hours. In

\*Formerly, clinical instructor in medicine, Yale University School of Medicine

†Associate professor of medicine, University of Cincinnati School of Medicine (on leave of absence)

1 case (Case 11), the diagnosis was doubtful. This patient had a definite compensated cirrhosis of the liver and a diabetic glucose-tolerance curve. We could not be certain that the disturbance in carbohydrate metabolism was not solely related to the underlying hepatic disease, but despite this fact the case was included in the series.

It was decided to classify the patients in two groups, comprising those with known precursors to diabetes and those with no known precursors. Inclusion in the former group was based on the factors of a family history of diabetes, of overweight and of age. The family history, which was gone into in great detail, was considered positive when a history of diabetes in the blood relatives, living or dead, was ascertained. An arbitrary 10 per cent increase in weight over that given in the height and weight table of the Association of Life Insurance Directors and Actuarial Society of America<sup>14</sup> was allowed. It was decided to include all patients over forty years of age in this group, because it was thought that these patients had reached the age when the incidence of diabetes increases. All but 2 of these patients were overweight.

The average age of the patients was thirty years, and the ages ranged from nineteen to fifty-four. Forty-three patients were men, and 1 was a twenty-four-year-old nurse. All the patients were white. Two were Jews, in neither of these did the diabetes begin after entry into the Service. In both cases, the diagnosis of diabetes had been made in civilian life, but the patients had been inducted into the Army. They were asymptomatic for two and a half and three years, respectively, at the end of which times the diabetes was rediscovered.

Two possible mechanisms suggest themselves by which psychogenic influences become capable of initiating diabetes. One of these is a functional neuroendocrine disturbance that gradually results in the development of diabetes. One would naturally expect that if this disturbance could be removed, the diabetic state would disappear or greatly improve, but no definite evidence of this sequence was seen. In many cases the diabetic state seemed to improve, but there was no certainty that this was not related to the better regulation of the diet that was possible in the Zone of Interior. The other mechanism is analogous to a trigger mechanism whereby the psychogenic factors initiate the diabetes and the condition, once it has begun, becomes permanent and irrevocable.

Menninger<sup>12</sup> sets down five requirements to which psychogenically induced diabetes should conform. These are an obvious psychopathic state evidenced prior to the development of the diabetic state, a mental picture quite different from the toxic state occasionally seen in hyperglycemia or hypoglycemia, a course of improvement in the mental picture paralleled by the glycemic and glycosuria levels,

with fluctuations of these as emotional upsets occur in the psychic life, indication of the metabolic disorder by a persistent glycosuria, — without dietary control or insulin, — retarded glucose-utilization curves of the blood sugar and a response to dietary and in some cases insulin therapy, and clearing of the diabetes on mental recovery, without the necessity of insulin or rigid dietary treatment.

Complete psychiatric appraisals were not possible in these patients, but they assuredly suffered no marked psychiatric disturbance during their stay at this hospital. Nevertheless, they continued to take insulin, although the amount could be decreased. This decrease could also be explained on the basis of better regulation of the diet. There was no convincing evidence that the diabetes improved on the patients' return to the security of this country, and consequently it is not believed that these cases conform to the criteria set down by Menninger.

In addition, although we are well aware of the dangers of attempting to draw conclusions concerning the incidence of diabetes based on our statistics, we believe that diabetes is no more frequent in the Army than it is in civilian life. This is significant, since a soldier's life involves every kind of psychogenic trauma, including anxiety, insecurity and fear of death, so that a consequent increase in the incidence of diabetes is to be expected. On the other hand, a study of the history prior to the onset of the condition impresses one with the fact that in some of these cases an upsetting incident preceded the development of diabetes. As listed in Table 1, this was noted in 2 patients (Cases 9 and 12). In both these patients there was a family history of diabetes. Among the patients in whom there were no known precursors (Table 2), some (Cases 29, 30, 31, 32 and 34) showed suggestive relations, whereas in others (Cases 36, 37 and 40), the relations were less clear. It is significant that none of these patients recovered a normal sugar metabolism after being released from the stress of combat and realizing that they would soon be separated from the military service by a medical discharge. Follow-up information obtained in 11 patients (Cases 5, 6, 8, 10, 14, 27, 28, 29, 30, 36 and 37) four to six months after their return to civilian life revealed no appreciable change in their diabetic status.

#### SUMMARY

A study was made of psychogenic factors preceding the onset of diabetes mellitus in 44 patients who were admitted to an army general hospital.

In no case was it possible to prove a direct causal relation between the stress incident to military service and the subsequent development of permanent diabetes.

TABLE 2 Data in Patients with No Known Precursors to Diabetes

CASE No	AGE yr	RELATIVES WITH DIABETES	HEIGHT	NORMAL WEIGHT lb	DATE OF ONSET	DATE OF HOSPITALIZATION	REGIME ON DISCHARGE	HISTORY OF ONSET
26	25	0	6 ft	188	Oct., 1944	Nov. 1944	C233-P110-F105 PZI 30 units RI 10 units	Gradual onset of polyuria, polydipsia, polyphagia and weight loss while overseas
27	37	0	6 ft., 1 in.	188	Dec., 1944	Jan. 1945	C235-P90-F130 PZI 25 units RI 8 units	Gradual onset of polyuria and polydipsia, with loss of weight of 20 pounds in Zone of Interior
28	22	0	5 ft., 8½ in.	162	Oct., 1944	Oct. 1944	C200-P80-F110 PZI 20 units	Gradual onset of polydipsia and dryness of mouth 3 wk. after being withdrawn from combat
29	36	0	6 ft.	182	July 1944	Aug. 7 1944	C200-P90-F90 PZI 18 units	Patient had severe emotional shock when buzz bomb struck company area. he became nervous and tired and began to lose weight in the next 10 days and developed polyuria and polydipsia.
30	21	0	5 ft., 8 in.	158	Sept., 1944		C200-P70-F80-PZI 20 units	Patient was wounded in action polyuria and polydipsia developed during subsequent hospitalization
31	29	0	6 ft.	170	Dec., 1944	Dec. 1944	C250-P100-F100, PZI 5 units	When patient was inducted, he was told he had nervous tremor; he developed frequency on voyage overseas, immediately placed in active combat, when symptoms increased and the patient lost weight, vomited and developed acidosis.
32	34	0	5 ft., 10 in.	165	Dec., 1944	Feb. 1945	C200-P90-F110 PZI 40 units	Patient noticed fatigue, increased thirst, and nocturia while lost behind German lines for 5 days, these continued after he made his way to the American lines; he developed irritation of the penis a month later glycosuria was found and he was hospitalized.
33	26	0	5 ft., 7½ in.	?	Mar., 1944	?	C150-P90-F100 PZI 18 units	Polyuria, polydipsia with gradual onset while overseas
34	34	0	5 ft., 10 in.	145	Jan., 1945	Mar. 1945	C225-P100-F90 PZI 14 units	Patient wounded in Nov. 1944, and had two operations; nervous and jumpy while in Replacement Pool.
35	24	0	5 ft., 8 in.	150	?	Dec. 1944]	C175-P90-F100 PZI 7 units	Routine urine examination revealed sugar on hospitalization for intercurrent illness
36	23	0	5 ft., 11 in.	160	Sept. 1944	Nov. 1944	C200-P90-F110 PZI 30 units	Patient was under considerable mental and physical strain while trying to complete certain military duties prior to return to Zone of Interior on furlough
37	26	0	5 ft., 6¾ in.	140	Oct., 1944	Nov. 1944	C200-P100-F100 PZI 40 units RI 20 units	Patient under considerable mental strain because of difficulties with commanding officer while overseas
38	24	0	5 ft., 8¾ in.	157	Apr. 1945	Apr. 1945	C200-P90-F90, PZI 15 units	Polyuria, polydipsia and weakness developed while awaiting assignment in a parachute infantry unit
39	26	0	6 ft., 1¾ in.	185	Jan., 1945	Jan., 1945	C200-P90-F100	Gradual onset of polyuria, increased thirst and nocturia while working in a general hospital overseas
40	26	0	5 ft., 5 in.	140	Jan., 1945	Apr., 1945	C260-P76-F114	Patient developed polyuria and polydipsia while taking infantry basic training
41	24	0	5 ft., 8 in.	150	July 1944	Apr., 1945	C200-P80-F120 PZI 20 units	Gradual onset of increased thirst and loss of 25 pounds in weight while overseas
42	34	0	5 ft., 8½ in.	168	Mar., 1945	May 1945	C250-P70-F80 PZI 20 units	Increased thirst and polyuria while waiting to cross Rhine with artillery outfit
43	21	0	5 ft., 6 in.	160	Feb., 1945	?	C200-P90-F100 PZI 30 units	Patient developed gas on stomach polyuria polydipsia and nocturia
44	24	0	5 ft.	104	July 1944	July 1944	Regular diet	Routine urine examination revealed sugar while overseas

by orchidectomy alone. Although 65 were improved clinically, 10 received no benefit whatever. Hamm<sup>3</sup> reported 5 cases all of which were helped by orchidectomy alone. These figures give an immediate improvement in 80 per cent of patients treated by orchidectomy alone.

There are those who favor estrogen therapy rather than orchidectomy. Kearns<sup>9</sup> treated 37 patients with stilbestrol, with improvement in 30. Kahle et al.<sup>10</sup> reported 7 patients benefited by stilbestrol alone, and of 12 patients so treated by Marquart and Flaherty,<sup>6</sup> 5 were improved. A case of spinal-fluid block relieved by stilbestrol alone was reported by Clarke and Viets.<sup>11</sup> Since approximately 75 per cent of patients treated with estrogens alone were improved, there appears to be little to choose between castration and estrogen therapy. Most writers believe, however, that the most spectacular and quickest beneficial results are obtained by orchidectomy. The issue is further confused by the fact that many authors have employed both castration and estrogenic therapy together.<sup>12</sup> It is obvious that more time must elapse before it becomes clear which form of treatment is the better.

Any hope that cancer of the prostate might be cured by endocrine therapy was dissipated long ago. All observers agree that the effects of such treatment are temporary and that sooner or later androgens from some source in the body again stimulate the cancer cells to activity. Regression of the primary growth and of metastatic lesions may be prompt and striking, and an almost unbelievable change for the better in the patient's physical condition may take place, but after months or a few years symptoms can be expected to reappear and the growth to become active again. It has been thought that the lesions that more closely resemble the adult gland respond best to treatment,<sup>13</sup> but others have found no correlation between the grade of malignancy and the length of relief afforded by treatment, and believe that lesions of higher grades of malignancy respond as well as, if not better than, those of lower grades.<sup>14</sup>

The expectation of life for those with cancer of the prostate, before orchidectomy or estrogen therapy was employed, was estimated by Bumpus<sup>15</sup> in 1926 from a study of 1000 cases at the Mayo Clinic. The average survival period was thirty-one months after diagnosis. Two thirds of those with metastases were dead nine months after their first treatment, and 58 per cent of those without metastases were dead in one year. In 1937, Welch and Nathanson<sup>16</sup> studied 204 cases of cancer of the prostate for life expectancy and reported that of 39 untreated patients, 25 per cent were dead in eight months, 50 per cent in twelve months and 75 per cent in twenty-one months after the onset of symptoms. Of the 175 treated patients, 25 per cent were dead in fifteen months, 50 per cent in twenty-six months and 75 per cent in forty-one months. They state

that the British Ministry of Health found the average duration of life in 30 untreated cancers of the prostate to be less than seventeen months after the onset of symptoms.

The improvement in life expectancy that has resulted from the newer methods of treatment is shown by the following figures. Seventy-five patients with prostatic carcinoma treated by orchidectomy and carefully followed were reported by Nesbit and Cummings<sup>7</sup> in 1944. One third had died and two thirds were alive twenty-one months after operation. Eighty-four per cent of the patients with metastases passed the nine-month period in which Bumpus<sup>15</sup> reported a survival rate of only 33 per cent. Eighty-seven per cent of the patients without metastases were alive after twenty-one months, as contrasted with a survival rate of only 42 per cent after one year in Bumpus's series. When compared with Welch and Nathanson's figures of 50 per cent of treated patients alive after twenty-six months, the 66 per cent of total patients treated by Nesbit and Cummings by orchidectomy and alive after twenty-one months is less striking. The average duration of life of 21 patients with metastases who died after castration was only 11.3 months, although many of them were doubtless in an advanced stage of their disease. From the Mayo Clinic, Emmett and Greene<sup>14</sup> reported that 66 per cent of 133 patients were living eighteen months after orchidectomy and that 78 per cent of those with metastases survived the nine-month period. This again shows an improvement over Bumpus's figures, but the fact that 44 per cent of the patients were dead within eighteen months is not so impressive when compared with the 50 per cent of treated patients dead in twenty-six months as reported by Welch and Nathanson before androgen control. There seems little doubt that endocrine therapy prolongs the lives of patients with cancer of the prostate, but it is not yet clear just how much can be expected in this direction, particularly when the natural course of the disease varies so greatly.

The question of when endocrine therapy should be instituted is still being debated. A questionnaire was sent to seventy urologists in an effort to settle this point.<sup>17</sup> The answers were revealing in showing the confusion that exists concerning when treatment should be begun. One third of the urologists questioned perform bilateral orchidectomy as soon as the diagnosis of cancer of the prostate is made. Most of the rest delay it until metastasis can be recognized by x-ray, symptoms or laboratory evidence. A few do not favor the operation. From their observations, Nesbit and Cummings<sup>7</sup> conclude that the maximum benefit to the patient is derived by delaying endocrine treatment until the onset of symptoms from advanced or metastatic lesions has occurred. Others<sup>12, 18, 19</sup> agree with this.

There appears to be no definite evidence that castration or estrogen therapy prevents metastases.

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## MEDICAL PROGRESS

## UROLOGY

## Carcinoma of the Prostate

FLETCHER H COLBY, M D \*

BOSTON

THE beneficial effects of a reduction of the male sex hormone (androgen control) in patients with carcinoma of the prostate were strikingly demonstrated by Huggins and Hodges<sup>1</sup> over four years ago. Since that time, a great many reports of the effects of castration and estrogen therapy on the malignant prostate have appeared. Although there is still no uniform opinion on the best method of treating this disease, there is a tendency toward agreement on certain points.

A wave of enthusiasm for castration in all cases of prostatic cancer followed these earlier reports. This was tempered by a few skeptics. On the other hand, castration and estrogen therapy have obviously been more effective in their immediate beneficial results than has any other treatment previously employed. The use of external or interstitial radiation has greatly decreased, and the partial removal of obstructing tissue by perineal operation has been largely abandoned in the treatment of prostatic cancer. From the many reports published during the last few years on series of cases of prostatic carcinoma treated in various ways, the questions arise whether castration or estrogen therapy is the better procedure, how effective and how permanent these methods are, and when these measures should be instituted.

There is fairly general agreement that the radical operation of Young, consisting of total perineal removal of the carcinomatous gland, including the capsule, prostatic urethra, bladder neck and seminal vesicles, is the only method that offers any expectation of cure. Objections to this procedure have emanated from those who believe that lymphatic extension has already taken place in practically every case of prostatic cancer when first seen, and

from those who point out that few patients present themselves early enough to make this operation practical. It is true that the cancer should not have spread beyond the prostatic capsule, or at the most should involve only the lower ends of the seminal vesicles, if the radical operation is to be undertaken. If the results of radical surgery are good, however, it would seem that the patients who are found suitable for it, no matter how few, should not be denied its advantages. From the Brady Urological Clinic at the Johns Hopkins Hospital, Colston<sup>2</sup> reported that 23 per cent of the patients admitted to that institution with carcinoma of the prostate were subjected to radical operation. Probably less than 5 per cent of similar patients seen in most other clinics are found suitable for this operation. Previous reports from the same source have emphasized the value of radical surgery in early cancer of the prostate and bear sufficient evidence of long-term apparent cure to justify its use. According to Nathanson,<sup>3</sup> the following percentages of five-year cures of early cases of prostatic cancer treated by radical perineal prostatectomy have been reported: Belt, 58 per cent, Young, 53 per cent, and Colston, 50 per cent. Such figures appear to refute those who hold an entirely pessimistic attitude toward any possibility of cure of prostatic malignant disease.

It is also generally agreed that the majority of patients with cancer of the prostate are immediately benefited by castration or estrogen therapy. Bum-pus et al<sup>4</sup> recently reported 25 cases treated by orchidectomy, with improvement in all but 1. Huggins et al<sup>5</sup> treated 21 cases by orchidectomy, with improvement in 15. Of 21 cases similarly treated by Marquart and Flaherty,<sup>6</sup> 11 were improved. Nesbit and Cummings<sup>7</sup> treated 75 patients.

\*Instructor in surgery, Harvard Medical School chief of the Urological Service, Massachusetts General Hospital



arrest the disease. In younger women in whom it is desirable to preserve ovarian tissue, localized excision of involved areas is advised. In women near the menopause, roentgen-ray irradiation of the ovaries usually causes the bladder lesions to disappear. If the lesions persist or progress after the removal of all ovarian tissue, segmental resection of the bladder wall is necessary.

RENAL CALCULI

Three years ago, a new technic for the operative removal of small stones in the kidney was described by Dees.<sup>25</sup> Since the recurrence of stones after pyelolithotomy is frequent and is due in many cases to failure to remove all small calculi at the time of operation, a method that helps to clear the kidney completely is of considerable importance. Dees's contribution may be regarded as a significant advance in the problem of renal calculi.

Following a prolonged, traumatic and apparently futile exploration of a kidney for a small elusive stone, as described by Dees, a blood clot was removed from the renal pelvis, within which the small calculus was entrapped. Impressed by this fortunate accident, he searched for a suitable coagulum to fill the renal pelvis and calices. Fibrinogen from human plasma fulfilled the requirements of a substance that would completely fill the interior of the kidney, clot quickly and firmly, not be harmful to the kidney and dissolve spontaneously. Fibrinogen solution is converted into a fibrin clot by adding thrombin. The thrombin used is a fraction of globulin derived from rabbit plasma. The coagulum formed is said to dissolve spontaneously in human urine at 37°C within eighteen to twenty-four hours. At operation the upper ureter and renal pelvis are exposed. The ureter is gently occluded and a small incision is made in the renal pelvis. A No. 12 French urethral catheter is put into the pelvis, and any urine present is aspirated. The pelvis is washed with normal salt solution and then with fibrinogen solution. The pelvis is filled with fibrinogen through the catheter while simultaneously one tenth as much of 2 per cent clotting globulin is injected through the wall of the catheter with a syringe and needle. After five minutes, a firm cast of the pelvis and calices forms. This is removed by enlarging the pyelotomy incision. The coagulum frequently extrudes itself or may be removed by forceps, and brings with it all small stones that lie free within the kidney. Animal experiments conducted by Dees showed that no harm was done to the kidney by the retained coagulum or its intro-

duction, and the procedure was carried out in 21 patients without demonstrable ill effect.<sup>26</sup>

We recently used the coagulum technic in a patient with multiple small stones in the kidney pelvis. The clot extruded itself intact on opening the pelvic wall, forming a perfect cast of pelvis and calices. All the calculi, including several small stones unsuspected in the preoperative x-ray films, were enmeshed in the clot. Air pyelograms assist greatly in determining beforehand whether this method is suitable, since unless the air surrounds all the stones in the calices of the kidney, the calculi are apt to be adherent and are not removed by the clot. Although this procedure has limitations, it has considerable value, and trauma to the kidney is minimal.

262 Beacon Street

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In Nesbit and Cummings's<sup>7</sup> series, 31 per cent developed metastases after castration, in Emmett and Greene's series<sup>14</sup> 35 per cent did so. On the merits of combined treatment, orchidectomy and stilbestrol, Herger and Sauer<sup>19</sup> recently expressed the opinion that orchidectomy preceded or followed by stilbestrol does not offer any advantages over castration alone. Stilbestrol when given to patients whose symptoms recurred after orchidectomy was seldom helpful. They observed temporary benefit in 15 patients who had been on stilbestrol for a long time and then were castrated, whereas 4 showed no response. They conclude that castration after estrogen therapy may be of value, but that estrogen therapy begun after castration has failed is seldom effective.

### DECAPSULATION OF THE KIDNEY

Opinions have varied considerably whether decapsulation of the kidney is beneficial in the treatment of certain renal conditions. The operation was advocated by Edebohls about forty years ago for chronic nephritis and was practiced for a while, but it soon lost its vogue because the results were disappointing. The benefits of renal decapsulation have been attributed to the production of a collateral circulation from the perirenal tissues, an increased blood supply from interruption of the sympathetic nerves and release of tension within the kidney. Whether such changes actually occur has been questioned. More recently decapsulation has been advised for renal lesions other than chronic nephritis, notably toxic changes due to bichloride of mercury poisoning, reactions from the sulfonamides and post-transfusion anuria. After a thorough review of this subject, Abeshouse<sup>20</sup> concludes that decapsulation has unquestionable merit in certain conditions and that the chief indications for its use are progressive oliguria and anuria. He advocates the operation in the nephrotic stage of chronic parenchymatous nephritis associated with uncontrollable edema and albuminuria, anuria from bichloride poisoning not relieved by other measures, anuria following sulfonamide therapy and post-transfusion anuria. Others who have had experience with these conditions, however, are not in agreement concerning decapsulation.

Deming<sup>21</sup> points out that although there is little difference of opinion concerning the chief indications for decapsulation, — anuria and oliguria, — there is no definite proof that the operation is the factor that increases the urinary output and that many patients recover who are not operated on. He is not at all convinced that patients with bichloride of mercury poisoning recover because of decapsulation. Several years ago, Talbott<sup>22</sup> expressed the following opinion concerning decapsulation of the kidney:

The subject of decapsulation is of interest in a general discussion of nephrotoxic agents, since this form of therapy

has been recommended in the treatment of anuria. It is my opinion that nothing is to be gained by decapsulating anuric kidneys. If resumption of urine flow follows decapsulation, restoration would probably have followed conservative treatment. Since decapsulation is an extensive operation and patients with anuria are acutely ill, additional insults may be fatal and are best avoided. Recently we had an unusual opportunity to study the effects of unilateral decapsulation in a young woman who developed anuria following a transfusion reaction. On the fourth day of anuria, the right kidney was decapsulated, and catheters were placed in both ureters. Resumption of urine flow began about twenty-four hours after operation. There was no difference, however, between the urine volume from the decapsulated kidney and that from the untouched organ. Six weeks later, after normal urine volume had been established for some time and the concentration of nonprotein nitrogen in the blood was almost normal, inulin and Diodrast clearances were done. The ureters were catheterized again so that each kidney could be studied separately. A marked reduction in the rate of formation of glomerular filtrate and in renal blood flow was observed. More significant was the comparison of the two kidneys. No striking difference between the kidneys was noted in any of the functions measured. A mathematical average of all functions, however, showed a slightly better performance by the untouched kidney in comparison with the decapsulated one. Our results are interpreted as implying that unilateral decapsulation in this patient had no beneficial action on renal function.

I know of no other observation on the effect of renal decapsulation so carefully controlled as this one. Since the patient mentioned above was operated on in 1942, I know of no other case of decapsulation for anuria at the Massachusetts General Hospital. There are, however, many who regard decapsulation as beneficial in the treatment of certain types of oliguria and anuria.

### HYPERTENSION AND NEPHROPTOSIS

Of 133 cases of nephroptosis reported by Braasch and Goyanna,<sup>23</sup> only 16 showed hypertension, and in none of these was the nephroptosis considered the etiologic factor. The majority of patients with nephroptosis had blood pressures that were average or below average. Any compression of the blood vessels of the renal pedicle that might arise from the ptotic kidney was considered to be unlike the changes described by Goldblatt.

### ENDOMETRIOSIS OF THE BLADDER AND URETER

Invasion of the bladder by endometrial tissue has been considered unusual, and only 58 authentic cases have been reported in the literature. Twelve additional cases reported by O'Connor and Greenhill<sup>24</sup> give one the impression that this condition is not so rare as was supposed. Cyclic bleeding, considered a typical symptom, was recorded in only two thirds of the patients, and gross bleeding occurred much less frequently than one would expect. The cystoscopic appearance of these tumors may or may not be that of so-called "chocolate cysts." They are described as elevated, congested and edematous, often with a bluish or blue-black cast. The tumor mass may increase during menstruation. Biopsy is an aid in their detection. Removal of the ovaries usually results in a disappearance of these lesions, but occasionally this step does not

that it was probably present and that there were two lesions of the gastrointestinal tract that need to be explained

For the moment let us say that she was pregnant and that her denial of pregnancy was false

DR. TRACY B. MALLORY It is only fair to say that, when presented with the results of the Aschheim-Zondek test, she changed her story

DR. CLIFFORD That also makes me change my story

With a lesion in that area of the stomach and another lesion elsewhere in the bowel, the first thing that comes to mind is Hodgkin's disease or lymphoma. A lymphoma can cause intermittent profuse bleeding, and it can involve as great an area of the stomach without extreme symptoms as was demonstrated in this case by x-ray examination. As I thought this case over, before I knew that she was pregnant, the positive Aschheim-Zondek test made me entertain one wild speculation, which I shall still mention, to explain multiple intestinal lesions without pregnancy. The Aschheim-Zondek test is positive without pregnancy with a chorionepithelioma or hydatid mole. These usually occur following a pregnancy, but there have been some rare cases of chorionepithelioma of extragenital origin, which presumably arose from teratomas, with metastases in the lungs, liver and brain and some in the intestine. The possibility of implants of a chorionepithelioma in the intestines is ruled out by her admission of probable pregnancy, as well as by the rarity of such a pathological finding. A Krukenberg tumor or colloid carcinoma, with implants in the lower intestine, should also be mentioned in passing. An interesting feature is that she had not had more signs of intestinal bleeding, this presupposes that the lesion was primarily in the wall and was invasive, perhaps a sarcoma. We have no proof that the mass noted on physical examination was a second tumor, which thereby forces me to depend on the x-ray evidence. I shall make a provisional diagnosis of a sarcomatous lesion in the antrum.

A PHYSICIAN Was a pelvic examination done on this woman?

DR. LAMAR SOUTTER Yes, she had an enlarged uterus, which was perfectly symmetrical and soft.

A PHYSICIAN Was there any connection between this and the abdominal mass?

DR. SOUTTER No, the abdominal mass was much higher than the record leads one to believe.

A PHYSICIAN Why does Dr. Clifford say sarcoma instead of carcinoma?

DR. CLIFFORD Primarily because of the extensive annular growth, the three-month story and the patient's age.

DR. MALLORY How would the appearance of this lesion in the stomach differ from that of an ectopic pancreas in the antrum, Dr. Lingley?

DR. LINGLEY Ectopic pancreatic tissue may produce a filling defect in the stomach that simulates carcinoma. The defect, however, is usually not annular but occurs rather more on one side.

DR. MALLORY Sometimes it produces an annular swelling of the sphincter, almost like hypertrophic pyloric stenosis.

DR. LINGLEY In this case there was ulceration of the mucosa, so that I have no hesitation in calling it a malignant lesion.

DR. SOUTTER Preoperatively we were quite uncertain what this patient had, but we thought that benign hypertrophy was a good bet. We made a large incision for exploratory purposes, and when we got in, we found a large mass at the pylorus. The peritoneum over it was glistening and intact. There were quite a number of enlarged nodes along the lesser curvature. The pylorus was obviously enlarged with growth of some sort, but whether or not it was pancreatic tissue we did not know. There was no muscular hypertrophy. We sent for a pathologist and gave him two nodes from along the lesser curvature. He could not make a diagnosis but thought that the lesion was probably benign. We believed that she should have a resection of the stomach because of obstruction. As there was a possibility that this was a malignant disease, it seemed that, to be adequate, the resection should be high. Since such a resection in that age group would not increase the mortality over that of a low resection, we did a high one. In order to get the anastomosis to lie transversely, with the best functional effect, we also had to remove a large amount of the greater curvature. We had difficulty at the lower end because the pancreatic tissue was close to the lesion, and we had to resect some of the pancreas with the specimen.

#### CLINICAL DIAGNOSIS

Carcinoma of stomach?

Sarcoma of stomach?

#### DR. CLIFFORD'S DIAGNOSIS

Sarcoma of antrum of stomach

#### ANATOMICAL DIAGNOSIS

Carcinoma of stomach with metastasis to one lymph node

#### PATHOLOGICAL DISCUSSION

DR. MALLORY We were unable to make a diagnosis on the gross specimen of the resected stomach. It did not seem to be as indurated or firm as we ordinarily expect a carcinoma to be. The possibility of lymphoma entered our minds. When the sections came through, it was quite obvious that the tumor was a scirrhous colloid carcinoma, which showed extensive infiltration of the wall of the stomach, and a single node out of the seven examined showed a small metastasis.

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

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#### CASE 32171

##### PRESENTATION OF CASE

A twenty-year-old unmarried woman entered the hospital because of progressive abdominal discomfort

Three months before admission the patient noted a tendency to belch, especially soon after the evening meal and through the night. The eructations increased in frequency, and a month later the belched gas became foul smelling. Six weeks before admission nausea and excessive salivation developed, especially in the early morning. At about the same time the patient began to have intermittent diarrhea. Between periods of diarrhea the stools were usually normal, but on three occasions foul, black, sticky feces were passed. There were also intermittent episodes of abdominal discomfort and generalized crampy pain. She had lost 9 pounds in the two months before admission, although the appetite had been good. Two weeks before admission spontaneous vomiting immediately after meals began and persisted thereafter, although some meals were retained.

The last menstrual period began two months before admission and was normal, previously they had always been regular. The possibility of pregnancy was denied.

On physical examination there was diffuse, slight, lower abdominal tenderness accentuated in the subxiphoid region. There was a small, slightly tender, freely movable mass in the right lower quadrant near the midline. The breasts were slightly nodular.

The temperature, pulse, respirations and blood pressure were normal.

The red-cell count was 4,400,000, and the hemoglobin 12.7 gm per 100 cc. The urine had a specific gravity of 1.028 and was normal. A guaiac test on the stool was negative. The gastric contents showed 12 units of total acid and no free acid before histamine and 11 units of total acid and 10 units of free acid after histamine. X-ray examination of the stomach was somewhat unsatisfactory because the patient vomited most of the barium, but a definite annular defect about 3 cm long was seen in the an-

trum. There was only a very narrow channel through the antrum and pylorus leading to an essentially normal duodenal bulb. The rugal folds were swollen. The film of the chest was normal. Gastroscopy failed to visualize any lesion, peristalsis was normal, and there was no evidence of rigidity of the stomach wall within the range of the gastroscope.

On the third hospital day her family physician reported that an Aschheim-Zondek test done the day before entry was positive. Her symptoms continued unchanged.

An operation was performed on the eighth hospital day.

##### DIFFERENTIAL DIAGNOSIS

DR MILTON H CLIFFORD From the story alone,—the skipping of a menstrual period and later a positive Aschheim-Zondek test,—one might have been justified in attributing the original symptoms to nervous indigestion precipitated by the emotional trauma and the subsequent symptoms of nausea and vomiting to the onset of pregnancy. Certainly the story is that of an increasing partial obstruction in the upper intestinal tract, presumably a pylorospasm from organic or functional causes, with periods of intermittent diarrhea suggesting irritation in either the lower intestine or in the large bowel. She passed foul, black, sticky feces. In the absence of taking iron or bismuth by mouth, the assumption is that the black feces represented bleeding and that she had had at least one episode of intestinal bleeding. This could not have been a constant oozing in view of the negative guaiac test noted later and in view of the level of hemoglobin, which, although not normal, was essentially so. There were two definite findings—x-ray evidence of a lesion in the stomach and a presumable lesion low in the abdomen on physical examination. Before we go farther, I should like to see the x-ray films.

DR JAMES R LINGLEY This is a definite prepyloric lesion, which extends up both curvatures and involves about 3 or 4 cm of the antrum. It is annular in type, and I think that the mucosa throughout this area is completely destroyed. There is also a suggestion of shelf formation along its upper margin.

DR CLIFFORD It is of interest that gastroscopy showed no abnormality, but of course the lesion was in the antral area, which is visualized with difficulty gastroscopically. The most significant negative information from the gastroscopic examination is that peristalsis was normal and that there was no sign of rigidity.

The second lesion that presented on physical examination, the small, slightly tender, freely movable mass in the right lower quadrant, near the midline, is consistent with a mass in the small bowel. It might, however, have been informative to have checked the colon by a barium enema. I am going to take that finding at its face value and assume

drome of which hepatic cirrhosis is probably the most important part. The physical findings of jaundice, an enlarged liver, ascites, edema and spider angiomas are consistent. The laboratory findings are also consistent, so far as the low serum albumin, the positive cephalin-flocculation test, the low vitamin A in the serum and the increased prothrombin time are concerned. With the data at hand there is no way of determining whether the anemia was due to the deficiency or to blood loss from hemorrhage. The blood chemical findings at the time of his episode of dyspnea and confusion on the sixth day after examination resemble those reported in experimental liver injury, and in such cases the acidosis is said to be due to failure of the liver to convert lactic acid to glycogen. The only unusual laboratory finding in this case is the high white-cell count, which I am unable to explain on the basis of infection, either in the liver or elsewhere, or as due to a recent acute hemorrhage. Although a low white-cell count is almost the rule in cases of what might be called chronic cirrhosis of the liver, I believe that with more acute episodes of liver-cell destruction leukocytosis may be present. I remember one case of portal cirrhosis in which there was an unexplained white-cell count of 18,000, when the patient came to autopsy no other cause for the increased count could be found.

Is it possible to explain this picture on any other basis than that of cirrhosis of the liver? The large size of the liver suggests a malignant tumor, presumably metastatic. We are not told the character of the liver edge, but I think that the manifestations of liver insufficiency are too marked to make this as a single diagnosis, in addition, there is no evidence of a primary focus. A palpable spleen would be helpful at this point as further evidence against the liver enlargement's being due to metastatic malignancy. The only possible type of new growth that would fit in here, I believe, is a primary hepatoma superimposed on cirrhosis, but there are no positive findings by which one could logically make this diagnosis. It does not seem necessary to consider obstructive jaundice or, except for the increased white-cell count, an infectious process in the liver.

If we accept the diagnosis of cirrhosis of the liver, the next question concerns its type. The episode of jaundice at the age of twenty-one, which persisted for two months, brings up the probability that this patient died of a toxic or nodular cirrhosis, with the primary insult to the liver occurring many years previously. The large size of the liver at the time of admission is somewhat against this diagnosis and in favor of the more frequent alcoholic cirrhosis, but we are often reminded in the exercises of the fallibility of physical diagnosis when it comes to determination of the size of the liver. Toxic cirrhosis, which is also called subacute or healed yellow atrophy and usually represents the end results of

repeated episodes of liver-cell damage or destruction, also explains the leukocytosis.

There are two final points. One is whether or not the patient had a duodenal ulcer either three and a half years before or at the time of death. I do not believe that this can be answered, since he did not have a gastrointestinal x-ray examination during his hospital admission, which, incidentally, might also have shown the presence of esophageal varices. The second point concerns the terminal episode that immediately preceded his death, and this seems to me to be a vivid example of massive gastrointestinal hemorrhage. This presumably took place from a ruptured esophageal varix, although again one wonders remotely about the duodenal ulcer. He did not vomit blood, but this I believe has been recorded not infrequently in patients dying from such a cause.

I propose a diagnosis of liver failure due to toxic cirrhosis, with death resulting from hemorrhage from a ruptured esophageal varix.

DR TRACY B MALLORY Dr Volwiler, would you care to comment about the impressions on the ward?

DR WADE VOLWILER The protein level of the blood, with the normal albumin-globulin ratio and the slightly lowered vitamin A level, did not help much with the diagnosis. They were just consistent with malnutrition.

We treated this man for acute liver disease, without success. He refused to eat, and regardless of whatever one gives in the way of supplements and fancy medicines, I am sure that the fundamental basis of liver-disease therapy comes down to a proper diet and enough of it.

I agree that an increased white-cell count can be explained by massive and diffuse hepatic-cell necrosis. In such patients white-cell counts up to 20,000 or 30,000 are not infrequent, with a preponderance of neutrophils, a shift to the left and many toxic granules.

#### CLINICAL DIAGNOSIS

Alcoholic cirrhosis of liver

#### DR SHORT'S DIAGNOSES

Toxic cirrhosis of liver, with esophageal varices  
Terminal gastrointestinal hemorrhage

#### ANATOMICAL DIAGNOSES

Cirrhosis of liver, alcoholic type.

Hemorrhages in lungs

Bronchopneumonia

Peritonitis, acute generalized early

#### PATHOLOGICAL DISCUSSION

DR MALLORY The autopsy showed cirrhosis of the liver. The liver at that time, whatever it may have been earlier, was small, weighing 1450 gm, perhaps 300 gm below what might have been ex-

DR CLIFFORD How much mucosal involvement was there?

DR MALLORY The mucosa was ulcerated away over the entire extent of the tumor.

Can you answer the question about the second mass, Dr Soutter?

DR SOUTTER There was no second mass

## CASE 32172

### PRESENTATION OF CASE

A fifty-five-year-old auto-supply dealer entered the hospital complaining of jaundice and abdominal swelling

At some indefinite period five or six months before admission the patient began to be troubled by "gas" in the abdomen and by increasing weakness. He continued to work until ten weeks before admission, when these symptoms, along with occasional nausea and vomiting, forced him to bed. Five weeks later he began having paroxysms of coughing and developed dyspnea. Two weeks before admission he became aware of a progressive uncomfortable swelling of the abdomen and of yellowness of the skin. He had never noticed any unusual color of the stools or urine. He complained of shooting pains in the arms and fingers and noticed tingling of the tip of the tongue. There had been marked wasting of the face, extremities and thorax, and an overall weight loss of some 15 pounds.

For ten or fifteen years the patient had consumed a fifth of a gallon of whisky daily. During that time his appetite was poor and he frequently went for a week at a time without eating any appreciable amount of food. He stopped drinking two weeks before admission.

Three and a half years before admission the patient entered another hospital because of gastrointestinal hemorrhage manifested by the passage of tarry stools. He received a blood transfusion and was discharged after a week, an x-ray diagnosis of duodenal ulcer having been made. There was no known gastrointestinal hemorrhage after that except for intermittent and, at times, fairly well marked bleeding from hemorrhoids. At the age of twenty-one years, the patient had jaundice, weakness and anorexia, which caused him to stop work for two months.

On physical examination the skin and scleras were moderately jaundiced. The tongue was beefy red, and the finer papillae were atrophied. A few fine crackling rales were heard at the base of the right lung. The protuberant abdomen bulged at the flanks, and there were a fluid wave and shifting dullness. The liver edge descended six finger-breadths below the ribs. A few spider angiomas were present on the skin of the chest and neck. There was moderate pitting edema of the legs and over the sacrum. All the extremities were weak,

and the outspread hands trembled. There were prominent internal and external hemorrhoids.

The temperature was 99.6°F, the pulse 125, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

The red-cell count was 2,850,000, with 88 gm of hemoglobin. The white-cell count was 33,700, with 88 per cent neutrophils. The urine showed a specific gravity of 1.016 and gave a + test for albumin and bile; the sediment contained 10 white cells and a rare red cell per high-power field. Urobilinogen was demonstrable in a dilution of 1:200. A stool gave a negative guaiac reaction. The serum bilirubin level was 3.4 mg per 100 cc direct and 4.8 mg indirect. Other blood chemical findings were as follows: nonprotein nitrogen, 21 mg per 100 cc; protein, 4.2 gm, with 2.3 gm of albumin and 1.9 gm of globulin, and vitamin A, 0.3 unit per cubic centimeter. A cephalin flocculation test was equivocal at twenty-four hours and ++++ at forty-eight hours. The prothrombin time was 33 seconds (normal, 19 to 22 seconds).

On the second hospital day 700 cc of clear yellow ascitic fluid was obtained. Anorexia and weakness persisted. On the sixth day the patient was found sitting up in bed breathing deeply. He was drowsy and confused, complaining of numbness in the hands and feet. The serum bilirubin had risen to 5.2 mg per 100 cc direct and 7.8 mg indirect, and the carbon dioxide level was 20.6 milliequiv per liter. The chloride was 98 milliequiv per liter, and the sodium 136.1 milliequiv. With intensive dietary and intravenous therapy his condition improved slightly over the course of weeks. Anorexia and apathy made it impossible for a satisfactory high-calorie intake to be maintained. The liver edge was felt to be definitely receding. On the thirty-second hospital day the patient gradually became markedly dyspneic and cyanotic. The pulse was unobtainable, and the blood pressure was 88 systolic, 76 diastolic. He was sweating and apprehensive and complained bitterly of abdominal distress. Attempts to pass a Levine tube were abandoned because the patient could not swallow and became even more cyanotic during the procedure. Respirations slowed and eventually ceased about six hours after the onset of the severe dyspnea.

### DIFFERENTIAL DIAGNOSIS

DR CHARLES L. SHORT With the possible exception of the episode of gastrointestinal bleeding that occurred three and a half years before this patient's admission, his entire medical history seems to point to disease of the liver. The story of a high alcoholic intake for ten or fifteen years and, perhaps more important, his periodically inadequate diet form a sufficient cause for the development of liver failure. The appearance of his tongue and the pains and weakness of his extremities are further examples of the development of a deficiency syn-

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## THE INADEQUACIES OF MEDICAL CARE

### III THOSE CONCERNING ITS QUALITY

ONE topic rarely mentioned by the medical profession in discussions concerning medical care is its quality. It seems to be assumed that, because the science of medicine has advanced as far in the United States as in any other country of the world, all licensed physicians are equally proficient. Such, unfortunately, is not the case, and many things must be accomplished before the matter can be corrected.

The first step is to be sure that all medical students receive an adequate education. Although it is true that the majority of substandard schools have been forced to close, and that all the states but one

do not permit graduates of such schools to take examinations for licensure, the fact remains that many thousands of graduates of substandard schools are in active practice. Undoubtedly some of these physicians give better medical care than do certain graduates of approved schools, but the majority of them do not. There has been no practical way in which any kind of check could be made on their activities, since the majority are not acceptable as staff members of recognized hospitals, a matter that is discussed in greater detail below.

A corollary of adequate medical education is the responsibility of the medical school and teaching hospital to turn out physicians whose training has been in accordance with the existing demand. Undoubtedly the majority of medical-school graduates aspire to become certified by one of the specialty boards, — in fact, 80 per cent of the 21,000 medical officers serving with the armed forces so stated in a poll taken two years ago, — but it is obvious that such a superfluity of specialists would not serve to the best interest of caring for patients. The bulk of the profession must be composed — as it always has been — of physicians who are trained to give general medical care and who are sufficiently intelligent and self-effacing to refer their difficult cases to the specialist. This type of medical education requires only about half the time necessary for qualification as a diplomate, and if an appreciable number of medical schools and teaching hospitals were to foster and promote such training, great benefit would accrue.

Secondly, some attempt should be made to control the various cultists who are licensed to practice their particular vocations in many of the states. Nothing short of a change in laws can remedy this situation, but one shudders to think of how many cases of tuberculosis and cancer remain unrecognized, because of this, until it is too late for effective therapy. In spite of her tardiness in finally refusing to accept applications for licensure from graduates of substandard medical schools, it is to the credit of Massachusetts that, to date, her legislators have refused to recognize cultists, other than osteopaths, and even they are required to take the same examination as do the graduates of regular medical schools.

pected in a man of his size. It showed a diffuse cirrhosis with an extremely fine type of granularity, the characteristic gross picture of the cirrhosis seen in people with severe alcoholic histories. That was further borne out microscopically. In the early stages of alcoholic cirrhosis, large livers with intense fatty infiltration are the rule, and in the later stages the fat frequently disappears, but in both stages a characteristic type of hyaline degeneration is found in the liver cells. This is present in the great majority of the alcoholic cirrhotics and is rarely seen in the livers of those who do not give a history of alcoholism or at least in whom the possibility of alcoholism can really be excluded. I think that one is justified without question in making a diagnosis of alcoholic cirrhosis here. In contrast to many cases that one sees in the late atrophic stage, the process was still extremely active. A great many of the liver cells were currently undergoing this peculiar

form of degeneration, and others were frankly necrotic. There were a great many foci of leukocytes about the necrotic cells, which fits in well with the elevated white-cell count.

The other features of the case were relatively unimportant. The spleen was not so much enlarged as one would expect in view of the chronicity of the story, it weighed only 250 gm. The heart was slightly hypertrophied. There were widespread hemorrhages throughout the lungs, which were probably due to liver insufficiency. The kidneys were essentially normal. There was terminal infection — a frank pneumonia and an early peritonitis.

DR. SHORT: Did he have esophageal varices?

DR. MALLORY: Small varices were found but apparently none had ruptured, since there was no blood in the stomach or intestines.



One hundred and thirty-five years ago the need for some outlet for the literary, scientific and social productivity of the Society other than the simple publication of its transactions was appreciated. Thus, on June 5, 1811, a committee was appointed "to ascertain, if possible, who are the conductors of a publication entitled *The New England Journal of Medicine and Surgery*, with a view to determine the expediency of incorporating the Communications of the Society in the said publication." It is assumed that the conductors preserved their anonymity, for no further report was forthcoming.

History tells us, however, that *The New England Journal of Medicine and Surgery and the Collateral Branches of Science*, a quarterly, continuing after 1826 as *The New England Medical Review and Journal*, was united in 1828 with *The Boston Medical Intelligencer*, which had been published as a weekly journal since 1823, to form *The Boston Medical and Surgical Journal* — a name of hallowed memory and a journal, we trust, of continuing and increasing usefulness, published since 1928 as *The New England Journal of Medicine*. Thus the publication record of the *Journal* stretches back uninterruptedly to 1812, when *The New England Journal of Medicine and Surgery* made its first appearance — an endurance record for the New World!

The Society continued to publish its transactions independently until 1914, although in 1847 its president, Dr Jacob Bigelow, proposed that when the permanent fund of the Society amounted to \$10,000 the income should be devoted to the publication of a journal. This matter was indefinitely postponed, but on July 1, 1914, a direct affiliation with *The Boston Medical and Surgical Journal* went into effect, whereby a special department in that journal was created, under the editorship of the secretary of the Society.

The question of ownership of the *Journal* did not reach an encouraging phase until 1920, when the Council voted to enter into negotiations for its purchase. The current owners proving receptive, the *Journal* eventually passed into the hands of the Society for the sum of one dollar and other, no doubt less obvious, considerations. The reorganization took place in April, 1921, and Dr Walter P Bowers became the managing editor.

During the first year of the Society's proprietorship of the *Journal*, all members were assessed five dollars to defray part of the costs of publication. They thus received, whether or not as individuals they wanted it, a six-dollar journal for a dollar less than the regular subscription rate. This assessment has gone down as the circulation and advertising rates have gone up, until finally in 1945, as our correspondent states, not only did the members of the Society receive the *Journal* without cost, but the periodical actually made money for the Society. The circulation of the *Journal* has increased from some 4500 in 1921 to over 18,000 in 1946.

The editors accept the probability that the precise terms in which the Treasurer's report is necessarily couched are somewhat misleading, but they have ordinarily neither the time nor the inclination to be greatly disturbed over it.

## MASSACHUSETTS MEDICAL SOCIETY

### MARKING OF PRESCRIPTIONS FOR HABIT-FORMING DRUGS

The following statement from the Massachusetts Board of Registration in Pharmacy relative to the proper marking of prescriptions for habit-forming drugs should be of interest to all practicing physicians.

MICHAEL A. TIGHE, *Secretary*

The Massachusetts Board of Registration in Pharmacy wishes to inform you that the Pure Food and Drug Division of the Federal Security Agency has recently ruled that Sections 502(d) and 503(b) relative to the marking of prescriptions ("Warning — May be habit forming") must be carried out to the letter of the law.

For your information, these sections of the law read as follows:

*Section 502.* A drug or device shall be deemed to be misbranded (d) If it is for use by man and contains any quantity of the narcotic or hypnotic substance alpha eucaine, barbituric acid, beta-eucaine, bromal, cannabis, carbromal, chloral, coca, cocaine, codeine, heroin, marijuana, morphine, opium, paraldehyde, peyote, or sulphomethane or any chemical derivative of such substance which derivative has been by the Administrator after investigation found to be, and by regulations designated as habit forming, unless its label bears the name and quantity or proportion of such substance or derivative and in juxtaposition therewith the statement "Warning — May be habit forming."

*Section 503.* (b) A drug dispensed on a written prescription signed by a physician, dentist or veterinarian (except a drug dispensed in the course of the conduct of a business of dispensing drugs pursuant to diagnosis by mail) shall if —

(1) such physician, dentist or veterinarian is licensed by law to administer such drug and

(2) such drug bears a label containing the name and place of business of the dispenser, the serial number and date of such prescription, and the name of such physician, dentist or veterinarian, be exempt from the requirements of Section 502 (b) and (c) and (in case such prescription is marked by the writer thereof as not refillable or its refilling is prohibited by law) of Section 502 (d).

These two sections are self-explanatory, but it should be emphasized that it is necessary to place on the container the following, "Warning — May be habit forming." This inscription is required on every prescription item, including refills if the prescribing physician does not bar a refill. In other words, the only time that the pharmacist does not put the "Warning — May be habit forming" label on a prescription is when the doctor marks the prescription "Not to be repeated."

A third difficulty arises from the fact that mere graduation from an approved medical school is no guarantee of an efficient and up-to-date practitioner. The science of medicine has advanced and is advancing so rapidly that a graduate of five or ten years is neglecting the majority of his cases of serious illness if he applies to them the knowledge that was his on graduation. He must constantly keep himself professionally "fit" — by reading, by refresher courses and by contact with his associates. This, of course, is much easier for the physician on the staff of a large hospital, particularly a teaching unit, but it is still the responsibility of all who consider themselves to be practitioners of medicine. Unfortunately, as previously mentioned, graduates of substandard schools, the very men who would benefit most by contact with others, are usually denied hospital privileges. One hospital in Massachusetts has already taken steps to remedy this situation. All such physicians within the community have been invited to attend ward rounds, staff meetings and clinicopathological conferences. Those who give evidence of a fair amount of medical knowledge and of a desire to improve themselves will be permitted to take patients to the hospital and to care for them, under supervision, except for major surgery and operative obstetrics. As a result, these men should show marked professional improvement, their patients will be assured adequate hospital facilities and the general health of the community should be raised. On the other hand, there will undoubtedly be some men who will scorn this help or who will be unable to profit by it, such practitioners obviously contribute little toward improvement of medical care. The adoption of this constructive scheme in other community hospitals deserves serious consideration, it has received the enthusiastic support of the Massachusetts Medical Society and the Massachusetts Hospital Association.

Another problem tied up with the quality of medical care concerns the question, Who is qualified to do what? Obviously a surgeon in a small community ordinarily should not perform a Wertheim operation, nor should he remove a tumor of the brain or lung. But there is nothing to prevent him from doing so if his regard for the well-being

of the patient is so slight that he refuses to refer the case to a properly qualified surgeon. The American College of Surgeons and the American Board of Surgery have done much in recent years to label those who have had adequate training in surgery, and even boards of surgical specialists have been established. But all this accomplishes little unless the layman is taught that what one surgeon is capable of doing is not necessarily within the ability of another.

The final inadequacy that lowers the quality of medical care is a lack of diagnostic facilities. If the modern physician is denied the help of x-ray, chemical, pathological and bacteriological laboratories, his ability to diagnose most of his cases of serious illness falls to a level that is comparable with that of the family doctor of fifty years ago, — if, indeed, it does not fall lower, — and treatment of the patient accordingly suffers. Such laboratories can be maintained only by groups of physicians, clinics and hospitals, and this is undoubtedly one of the chief reasons why recently graduated physicians shun small cities and rural communities. The banding together of physicians in groups and the establishment of well equipped health centers and hospitals in areas that need them would do much to relieve the situation.

Several of the factors contributing to the quality of medical care concern state boards of licensure and departments of health. On the other hand, two of them — keeping professionally "fit" and practicing according to one's ability — are the direct responsibility of the practicing physician. Undoubtedly, however, the health of the Nation would be improved if the layman could be taught how to obtain the medical care that he specifically needs.

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## QUARTER CENTURY OF PROGRESS

A LETTER appearing elsewhere in this issue of the *Journal* serves at least to call attention to one interesting fact, namely, that the year 1946 marks the twenty-fifth anniversary of the Massachusetts Medical Society's ownership of the *Journal*. It may not be amiss to state that they have been years of mutual progress.

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## LOW-SODIUM DIET AND FREE FLUID INTAKE IN THE TREATMENT OF CONGESTIVE HEART FAILURE\*

### A Preliminary Report

WILLIAM C BRIDGES M D,† EDWIN O WHEELER, M D,‡ AND PAUL D WHITE, M D §

BOSTON

TRADITION is hard to break. Doubtless since the time of Adam, dropsy has been traditionally treated by the limitation of fluid intake, a natural result of the observation of the accumulation of water in the body tissues. Despite the assembly of clear-cut evidence in laboratory and clinic that restriction of common salt and of sodium in any form is much more important than is restriction of water, the practical application of this idea in effective form has been extremely slow. In a few places in this country where knowledge along this line was far more advanced than elsewhere, the usefulness of this treatment was appreciated, but the lag in the way of general acceptance—or rather, of adequate distribution—of this valuable information has been great, owing in part, doubtless, to the distractions of World War II.

The custom of late years at the Massachusetts General Hospital of casually advising a low-fluid and low-salt intake for congestive heart failure has during the past year given way to the far more successful application of a low-sodium and free fluid intake. In the fall of 1944, we were prompted to adopt this procedure on reading of Lyons's<sup>1</sup> experience in New Orleans following the vigorous report of Schemm,<sup>2,3</sup> who in turn was stimulated by his former preceptor, Newburgh.

Evidently, the secret of the success of this treatment in many cases is not merely to give a so-called "low-salt" diet, which may contain anywhere from 3 to 6 gm of sodium chloride, but to give a low enough salt intake, which may need to be as little as 2 gm or even less. This in turn allows one to permit, in fact to encourage, free intake of fluids for the relief not only of edema but also of thirst. The heart is able to support the increase of fluid intake, despite former fears, and the kidneys are

able to work much more effectively. Nor is it necessary to carry out this treatment in the hospital in all cases, although it is usually best to begin here; ambulatory patients can follow the regimen at home if properly instructed and if able to secure such an important item in the diet as salt-free bread. The amount of salt in ordinary bread alone, especially in the case of habitual bread eaters, is apparently sometimes great enough to make the difference between the persistence and the clearing of edema. Moreover, one should not wait for dropsy or even slight grades of systemic edema to appear, dyspnea and pulmonary edema are likewise helped, and the salt restriction may be usefully applied early in the treatment.

That sodium chloride plays a leading part in the development of edema was pointed out in 1901 by Achard and Loeper.<sup>4</sup> These investigators fed 10-gm samples of salt to patients with heart trouble and found that it was not excreted in the urine in twenty-four hours, as it was in certain other patients without heart disease, nor was the blood level of sodium chloride increased. From this they concluded that the ingested salt contributed to the edema. This experiment was not utilized in the treatment of cardiac edema until 1903, when Merklen<sup>5</sup> treated a group of edematous patients and nephritic patients with a milk diet without extra salt. He chose milk for this diet entirely because of its low salt content. The edema cleared under this regimen. Karell<sup>6</sup> had found in 1866 that a diet of 600 to 800 cc of milk a day was helpful in the care of edematous cardiac patients but he had little knowledge concerning the mechanism of its beneficial effects. Another study at about the same time as Merklen's, made by Vidal and Lemierre<sup>7</sup> and conducted in the same kind of patients, suggested that fluid intake need not be restricted to the extremely low levels set by Karell, for in their patients 3000 cc. of milk was permitted a day, without the reduction of the efficacy of the treatment. Thus, one of

\*Presented before the New England Heart Association November 26, 1945.

†Commonwealth Fund Research Fellow Massachusetts General Hospital, 1945-1946.

‡Graduate assistant in medicine, Massachusetts General Hospital.

§Physician, Massachusetts General Hospital.

## DEATHS

**ELLIOTT**—John J Elliott, M D, of West Roxbury, died March 29. He was in his fiftieth year.  
Dr Elliott received his degree from Hahnemann Medical College and Hospital of Philadelphia in 1921. He was a member of the New England Obstetrical and Gynecological Society and the American College of Surgeons.  
His widow survives.

**PIPER**—Frank J Piper, M D, of Framingham, died April 4. He was in his forty-ninth year.

Dr Piper received his degree from Tufts College Medical School in 1924. He was a veteran of the Southwest Pacific, having seen service as a flight surgeon at Guadalcanal, Admiralties and the Philippines. At the time of his death Commander Piper was on terminal leave after serving nearly four years in the Navy Medical Corps. Before entering service he was president of the staff and assistant to the surgical service of the active staff of the Framingham Union Hospital.

His widow, three daughters, his parents and a sister survive.

**ROSENAU**—Milton J Rosenau, M D, of Chapel Hill, North Carolina, died April 9. He was in his seventy-eighth year.

Dr Rosenau received his degree from the University of Pennsylvania School of Medicine, Philadelphia, in 1889. For twenty-five years he was connected with Harvard Medical School, first as professor of preventive medicine and hygiene and later as professor of epidemiology at the Harvard School of Public Health. From 1913 to 1922 he was director of the School of Public Health of Harvard University and the Massachusetts Institute of Technology. He was a world renowned authority on preventive medicine and sanitation, and since 1935 had been director of the University of North Carolina School of Public Health. He was a fellow of the American Medical Association and a member of the Association of American Physicians and the Society of American Bacteriologists.

His widow, a son, a daughter and a stepson survive.

MASSACHUSETTS DEPARTMENT  
OF PUBLIC HEALTH

## NOTES

John J Poutas, M D, M P H, has resumed his duties as director of the Division of Local Health Administration, Massachusetts Department of Public Health, having returned from overseas duty in the European Theater. Prior to returning to this country, Lieutenant Colonel Poutas served as chief of the Epidemiology Branch of the Preventive Medicine Division, Office of the Theater Chief Surgeon. His duties will include supervision of the eight district offices of the department and the nursing, nutrition, social-service and sanitation bureaus.

Roy F Feemster, M D, recently acting director of the Division of Local Health Administration, Massachusetts Department of Public Health, has returned to his former position as director of the Division of Communicable Disease.

Dwight J Mulford, Ph D, has been appointed laboratory chief of the Blood Processing Laboratory in the Division of Biologic Laboratories, Massachusetts Department of Public Health. This laboratory is especially designed for the fractionation of blood plasma into albumin, immune serum globulin, fibrin foam, fibrin film and other fractions of value in medicine, surgery and public health.

Otto C Yens, M D, has been appointed supervisor in charge of Crippled Children Services in the Massachusetts Department of Public Health. Prior to his appointment, Dr Yens held the rank of lieutenant colonel in the Medical Service of the 117th Evacuation Hospital, United States Army.

Ruth Alida Thomas, M A, C P H, has joined the staff of the Bureau of Health Information, Massachusetts Department of Public Health. Miss Thomas was formerly assistant professor in the Department of Hygiene and Bacteriology, Smith College. She also served as consultant in the Medical

Intelligence Branch of the Preventive Medicine Division, Office of the Surgeon General, United States Army.  
Alexander A Robertson, formerly chief sanitary officer with the Newton Health Department, is now serving with the Massachusetts Department of Public Health as supervising health-district sanitary officer.

John B Skinner, M S, has been appointed director of the Division of Occupational Hygiene of the Massachusetts Department of Labor and Industries. Mr Skinner has been an engineer with the department since 1941. He succeeds Mr Manfred Bowditch, who retired from state service to assume the position of field director of the Saranac Laboratory, Saranac Lake, New York.

## CORRESPONDENCE

## THE JOURNAL PAYS ITS OWN WAY

*To the Editor* Why should not the *Journal's* financial success be fully recognized? Despite the fact that the members of the Massachusetts Medical Society have always received their copies of the *Journal* at a figure below the usual subscription rate, even from the earliest years of the Society's ownership, the annual report of the Treasurer has consistently ignored this basic fact and presented the fiscal affairs of the *Journal* as if the publication were run at a loss, the deficit being made up by a benevolent grant in the form of an appropriation by the Society.

It appears to me high time that the members of the Society realize that they have never paid full rates for their subscriptions, that their per capita annual assessment (call it "appropriation" if you like) has steadily decreased under the administration of two able managing editors, Dr Walter P Bowers and Dr Robert N Nye, and that in 1945 not only did they receive their copies of the *Journal* without cost, but the *Journal* actually made money for the Society. Let us give credit where credit is due and stop speaking, writing and thinking of the *Journal* as if it were a drain on the Society's resources.

266 Beacon Street  
Boston 16

JOSEPH GARLAND, M.D

## NOTICES

## ANNOUNCEMENTS

Dr F H Capodici, having been released from military service, announces the opening of an office for the general practice of medicine at 247 Harvard Street, Dorchester.

Dr Leo J Cass, having returned from military service, is resuming the practice of internal medicine at 1101 Beacon Street, Brookline, and 20 Ridgfield Road, Winchester.

Dr Lewis S Pilcher announces his return to the practice of general surgery with offices at 43 Parker Street, Newton Centre, and 12 Bay State Road, Boston.

Dr George C Prather, having returned from military service, announces the reopening of his office for the practice of urology at 1180 Beacon Street, Brookline.

## NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Harvard Club of Boston on Friday, May 17, at 5 30 p m. Dr A C Christie will present the Holmes Annual Lecture, his subject being "The First Fifty Years of Radiology. The elements that have contributed to its growth as a great medical specialty."

NEW ENGLAND HOSPITAL FOR  
WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, May 2, at 7 15 p m in the classroom of the Nurses' Residence. Miss Bernice W Billings, R N, will speak on the subject "Program of the Boston Tuberculosis Association." Dr Elizabeth O'Neil will be chairman.

(Notices continued on page xv)

place, no salt or soda is to be used in cooking or at the table, and one should not employ salt substitutes that contain sodium in any form. Second,

The advantages of this form of treatment are threefold. It frequently enables one to control edema that cannot be controlled with the usual

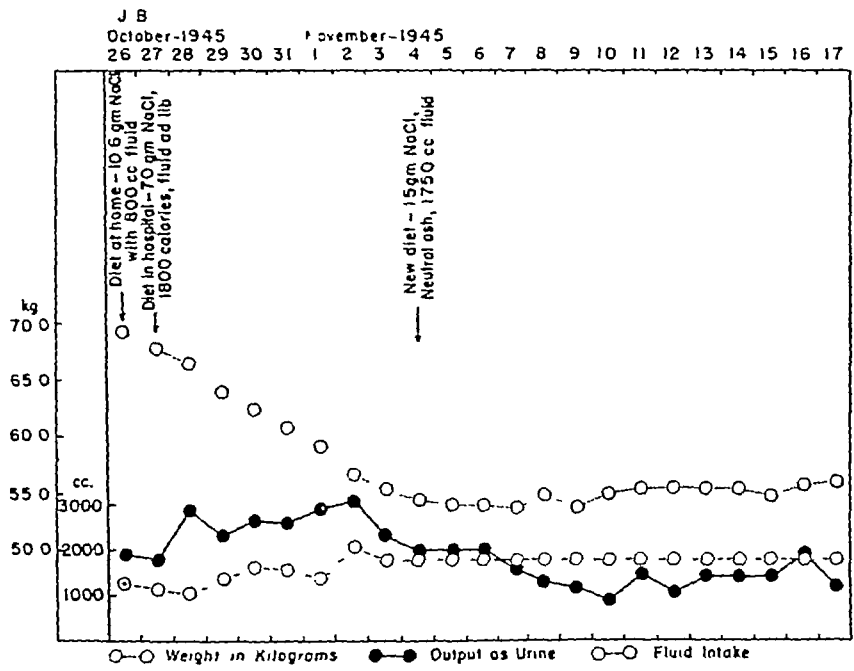


FIGURE 2

unsalted butter or butter that has been washed free from salt may be used, bread and salad dressings must be prepared salt free. Lastly, medicines

measures — that is, rest, digitalis and acid-forming and mercurial diuretics. It diminishes the frequency with which mercurial diuretics must be given,

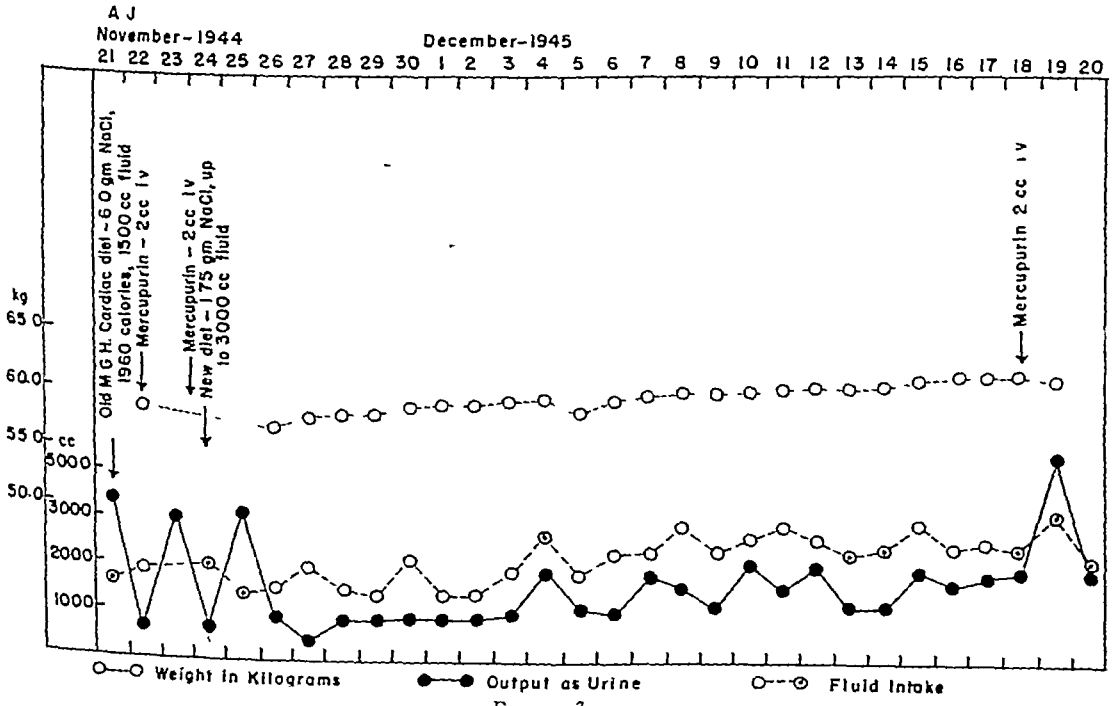


FIGURE 3

for gas and indigestion must not contain sodium, calcium salts are helpful as substitutes

indeed, these diuretics can frequently be entirely eliminated. Lastly, it enables patients to take

their patients, who had marked edema, could tolerate this amount of milk a day when salt was withheld from the diet (Fig 1)

As is widely known, however, even up to the present time edematous patients have in general been treated by the restriction of both salt and water. This was true at the Massachusetts General Hospital. Prior to the latter part of 1944 patients with congestive heart failure were treated with a diet containing 4 to 6 gm of sodium chloride a

to 6000 cc a day — and a low-sodium, neutral-ash diet as a means of controlling cardiac edema. He believes that the reaction of the diet is extremely important — in other words, that it is more helpful to keep the pH of the diet within limits than its sodium content.<sup>3</sup>

#### PLAN OF TREATMENT

During the past year we have treated patients with congestive failure with a diet quite low in

DATES	VOLUME D'URINE émise en 24 h	CHLORURE de sodium	URÉE	POIDS	ALIMENTATION	ETAT GENERAL
	lit			kil gr		
25 mai	2 150	6 90	25 80	"	3 litres de lait.	Oedème en voie de décroissance considérable
26 —	1 900	6 20	26 32	"	—	
27 —	2 100	6 85	26 80	"	—	
28 —	2 100	6 80	29 60	"	—	
29 —	1 950	7 00	28 30	"	—	
30 —	2 100	7 60	23 80	"	—	
31 —	2 000	7 50	24 50	70 200	—	
1 <sup>er</sup> juin	1 600	8 90	21 40	70 200	Lait, 3 lit pain, 120 gr , café, 500 gr biscuits 4 + NaCl, 10 gr	Reprise des œdèmes Oedème pulmonaire.
2 —	1 550	6 92	25 10	70 400	—	
3 —	2 000	10 90	22 20	70 200	—	
4 —	1 550	13 07	23 60	70 100	—	
5 —	2 000	19 20	31 00	70 600	—	
6 —	2 000	12 06	25 60	70 100	—	
7 —	1 500	9 04	28 20	71 300	—	
8 —	2 200	13 20	30 80	71 800	—	Gros œdème des jambes Oedème pulmonaire, œdèmes diminués
9 —	2 000	10 80	26 50	72 400	—	
10 —	2 000	11 90	30 20	72 600	Lait, 3 lit , pain 120 gr , café, 120 gr , biscuits 4, NaCl cessé	
11 —	3 200	11 05	32 60	72 900	—	Disparition des œdèmes
12 —	"	"	"	70 600	—	

FIGURE 1

day, and the fluid intake was restricted to 1000 to 1500 cc a day.

In 1934, Newburgh and Lashmet<sup>8</sup> studied the edema of nephritic patients. They pointed out the fallacy of restricting water in its treatment and the value of restriction of sodium as a means of limiting extracellular fluid.

Investigation of the relation of salt and water to the control of cardiac edema was not adequately reported further until 1941, when Schroeder<sup>9</sup> clearly showed that sodium was the important factor to be considered, and that provided its intake was held at low levels, the water intake could be raised to 4000 cc a day without the formation of more edema. This problem was also considered by Proger et al,<sup>10</sup> by Ellis<sup>11</sup> and more recently by Schemm.<sup>2,3</sup> The last-named worker advocates the use of extremely large rations of water — 5000

sodium chloride, in addition to the usual digitalis and diuretics. Before a consideration of the advantages and disadvantages of the low-sodium diet is undertaken, its composition should be presented. To begin with, the diet used in the treatment of patients with congestive failure has contained about 700 mg of sodium in an amount of food equivalent to 1800 calories. If the food tastes too flat, patients are allowed ammonium chloride in the salt shaker in the place of sodium chloride. The diet has yielded a neutral ash, although its reaction probably has little significance, since ammonium chloride is given. In the body the ammonia forms urea and the chloride is set free to neutralize the excess sodium. We have not attempted to balance alkaline-forming and acid-forming foods.

There are certain precautions that must be strictly adhered to in following such a plan. In the first

50 mg per 100 cc. He was digitalized and given the earlier cardiac diet of this institution, which contained 6 gm of sodium chloride a day. Fluids were restricted to 1500 cc a day. Under this regimen, however, there was little change in the patient's condition and the response to Mercupurin was poor. On the 7th hospital day, he was placed on the low-sodium, neutral-ash diet and the water intake was increased to 3000 cc a day. The edema cleared rapidly and the fluid in the left pleural cavity almost disappeared. The nonprotein nitrogen decreased to 36 mg per 100 cc. The patient was discharged to a nursing home on the 17th day, 9 days after the neutral-ash diet and increased water intake had been begun. He has continued to do well from the standpoint of his congestive heart failure.

CASE 4 (Fig 5) A 60-year-old baker with coronary and hypertensive heart disease had had congestive failure since 1943 and for many months had required weekly mercurial diuretics, in addition to his acid-forming diuretics. Besides this treatment he had followed a salt-poor diet and had restricted his fluid intake to 800 cc a day. He continued to feel miserable and complained of epigastric distress on this regimen. The mercurial injections were followed by marked prostration, lasting for several days after each injection. On March 22, 1945, he was started on the low-sodium, neutral-ash diet and was allowed fluids freely. Since then he has felt a great deal better and has required no mercurial injections.

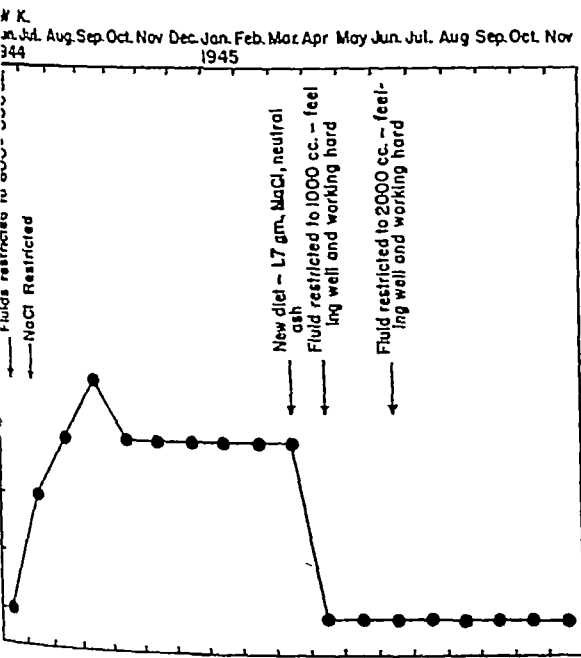


FIGURE 5

His sleep has been greatly improved, and he has been able to work every day, whereas formerly his activity had been markedly restricted. Prior to the initiation of this regimen he had great thirst and found it extremely difficult to restrict his water intake. He is no longer troubled in this way and continues to get along comfortably on the same small amount of fluid a day.

Comment. This case shows how successful this form of treatment may be in an ambulatory patient.

CASE 5 (Fig 6) A 59-nine-year-old woman had had hypertensive heart disease with congestive heart failure for 4 years. She required mercurial injections weekly to

control her edema. On February 26, 1945, she was admitted to the Phillips House with slight pitting edema of the ankles and hepatomegaly. The low-sodium, neutral-ash diet was prescribed, and water was given up to 3000 cc daily. The

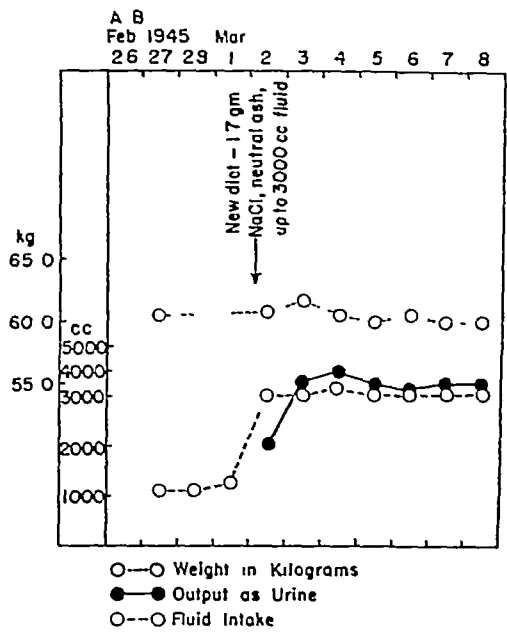


FIGURE 6

edema cleared on this form of treatment, and the patient required no mercurial injections for the 10 days she was in the hospital. Subjectively she felt a great deal better.

SUMMARY

Restriction of sodium to levels of 700 to 1000 mg (equivalent to 1.75 to 2.63 gm of sodium chloride) every twenty-four hours is helpful in the control of certain cases of congestive heart failure in which digitalis and mercurial diuretics are ineffective or not entirely satisfactory.

Water may be given freely, provided that the sodium intake is held to a minimum. Large water intakes may be of advantage in the elimination of edema, but this is probably a temporary phenomenon.

This regimen does not replace rest, digitalis and diuretic therapy but is a valuable adjunct to the treatment of obstinate congestive failure. In general, it has not been adequately used.

Five representative cases are reported.

The authors express their appreciation to Miss Shirley Wells for her help in arranging and analyzing the diets used in this study.

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more water than they otherwise could. Frequently those treated by the old regimen have been extremely thirsty.

There are also disadvantages, however. The chief of these are that a few patients find it difficult or impossible to obtain such a diet, especially those who eat their meals in boarding houses and restaurants, and that patients frequently complain of the flat taste of food, particularly during the early stages of the diet. Although these criticisms are difficult to overcome, the marked relief that patients often obtain from their distressing cardiac symptoms, notably dyspnea and insomnia, and from frequent mercurial injections overweighs these disadvantages.

We are not as yet in a position to confirm Schemm's belief that a water intake of 5000 to 6000 cc a day is more beneficial than one of 2000 to 3000 cc, but we are sure that the water intake formerly recom-

function. For example, if a given renal mechanism can concentrate urine to a specific gravity of only 1.010, it will require at least 3000 cc of water a day for the kidneys to eliminate the metabolic waste products in twenty-four hours. Should the patient develop an intercurrent infection, even larger amounts of fluid will be required to take care of this loss through evaporation from the skin and lungs.

## RESULTS

So far we have studied the effect of the low sodium diet on 64 patients, and have encountered varying degrees of success. Seventeen patients obtained much help, 15 moderate benefit, 8 slight benefit, and 7 no benefit. In the remaining 17 cases, either the patients were unco-operative or insufficient data regarding their response to the diet are available. Five cases will be briefly reported to illustrate the effect of this regimen.

**CASE 1 (Fig 2)** A 67-year-old man was admitted to the hospital in 1935 with a diagnosis of acute myocardial infarction. During convalescence from this illness he developed congestive failure. He was treated for this with digitalis, which he has continued to take. In the fall of 1942, he developed ankle edema, which has persisted up to the present time. In December, 1944, he developed ascites, which required abdominal paracentesis. Since that time he has had to have several paracenteses for recurring ascites.

The patient was readmitted to this hospital on October 26, 1945, with marked ascites, ankle edema and pulmonary edema. An analysis of the diet that he had been receiving at home indicated that he had been taking 10.6 gm of sodium chloride and 800 cc of fluid a day. He was put on a regular house diet containing 2 gm of salt a day and 1800 calories and was allowed as much water as he desired. He was permitted to continue taking 0.1 gm of digitalis a day, as he had been doing at home. Under this treatment he had marked diuresis and his general condition markedly improved, with disappearance of both the ankle edema and the ascites. On the 10th hospital day, — 8 days after he had been put on the diet containing 2 gm of salt, — the daily amount of sodium chloride was further decreased to 1.5 gm and the daily water intake was fixed at 1750 cc. Owing to the fact that the patient had already lost most of his edema, this had little new effect.

**Comment** This case illustrates extremely well how, in some cases, edema can be controlled simply by lowering the salt content of the diet.

**CASE 2 (Fig 3)** A 39-year-old truck driver had a pericardial resection for constrictive pericarditis in October, 1944. Following the operation he continued to require Mercurpurin every other day for anasarca, and this, as is frequently the case, was extremely fatiguing. In addition to this complaint, he had cramplike pains in the epigastrium following each injection of Mercurpurin. On November 24, he was placed on a low-sodium, neutral-ash diet and the water intake was increased from 1500 to 2500 cc a day. After he had been on this form of treatment for 23 days without mercurial injections, the edema decreased slightly and the breathing improved. The weight showed a slow increase, apparently because of a normal increase in body tissue. The patient was discharged in December.

He has continued to follow the diet and to maintain the fluid intake at 2500 cc a day. When last seen in July, 1945, he had considerably improved and had required Mercurpurin injections only four times in the last 6 months.

**CASE 3 (Fig 4)** A 73-year-old man had had hypertensive heart disease since 1943. In January, 1945, he developed congestive failure and was admitted to the Baker Memorial Hospital. On admission he had moderate ankle and sacral edema and a left hydrothorax. The nonprotein nitrogen was

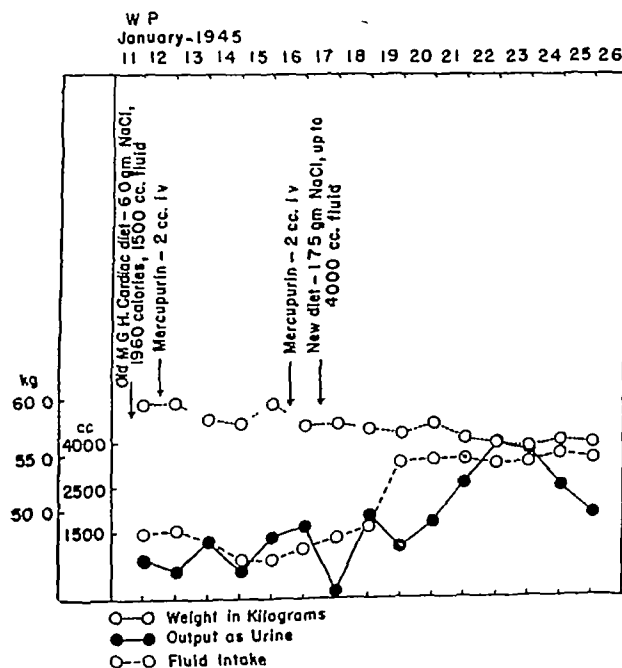


FIGURE 4

mended was often distinctly inadequate. The optimal amount of water in twenty-four hours on such a regimen has not been established, and we ourselves have not as yet adequately investigated this subject. The restriction of fluid as practiced in the past does not seem to have a physiologic basis. There are strong indications that under certain conditions, notably in cases in which there is a diminished renal function and the kidneys can no longer concentrate the urine to a specific gravity great enough to eliminate the waste products of metabolism in the normal volume of urine, a daily intake of water higher than 1500 cc is essential. Cardiac patients frequently have diminished renal



untreated and when they were treated by the ingestion of 1 ounce of whisky immediately at the onset of the attack was repeatedly measured. The amount of work that could be performed before pain was precipitated was determined in 21 patients at varying intervals up to ninety minutes after a

Five patients had at some time in the past attempted to obtain relief from attacks of angina pectoris by drinking whisky. One had obtained no relief, the remaining 4, however, believed that whisky had been beneficial. The following examples illustrate their experience. One patient (I K),

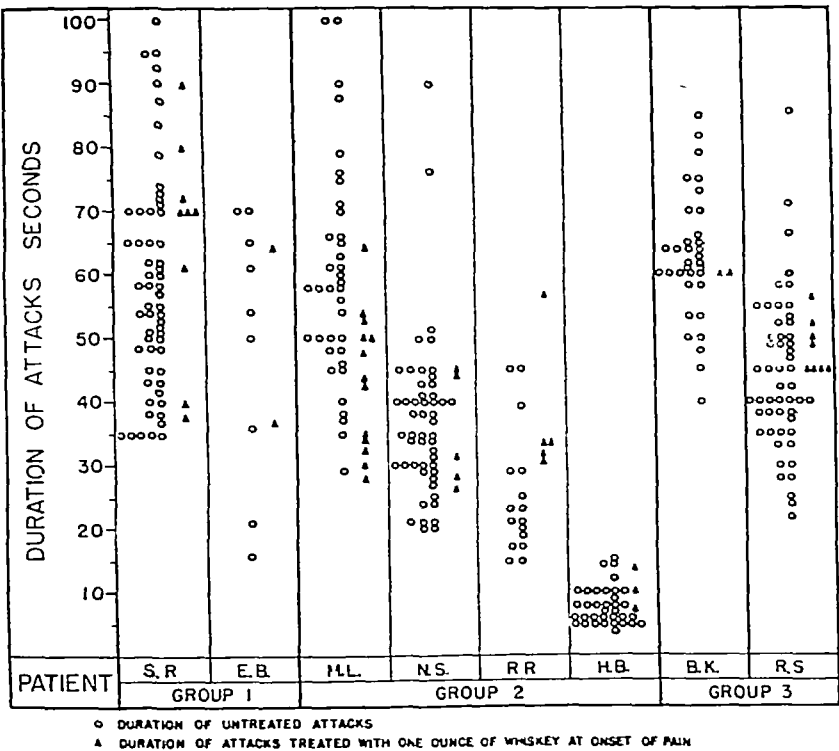


FIGURE 1 Duration of Attacks of Angina Pectoris

single 1-ounce dose of whisky, and this was compared with the usual performance of the patient while on ineffective or placebo medication. The amount of work that could be performed before pain was precipitated was determined in 9 patients who had taken 1 ounce of whisky four times daily for one week, including the morning of the test. Lastly, to demonstrate a possible reflex effect of alcohol, the amount of work required to precipitate pain was determined in 8 patients who exercised while holding 1/2 ounce of whisky in the mouth.

RESULTS

Effect of Alcohol on Duration of Attacks of Angina Pectoris

One patient (M.L.) whose untreated attacks averaged sixty-two seconds in duration demonstrated a decrease in the duration of pain to an average of forty-six seconds when given 1 ounce of whisky immediately at the onset of an attack (Fig 1). In the remaining 7 patients, no measurable effect occurred (Table 1 and Fig 1).

after developing chest pain, walked for fifteen minutes to obtain a drink of whisky, relief occurred five minutes after ingestion of the liquor and the cessation of walking. Another patient (R.S.) ob-

TABLE 1 Effect of Whisky on Duration of Angina Pectoris Induced by Standardized Exercise-Tolerance Test

NAME	SEX	DURATION OF PAIN			
		RANGE		AVERAGE DURATION	
		Untreated	Treated by Whisky	Untreated	Treated by Whisky
		sec	sec	sec	sec
B.K.	M	60-65	49-60	62	59
N.S.	M	50-40	31-43	36	35
S.R.	M	50-70	40-72	59	65
R.R.	M	15-25	32-34	24	33
R.S.	M	35-50	45-30	44	45
E.B.	M	35-65	36-64	49	50
H.B.	M	7-10	7-13	8	10
M.L.	M	45-65	35-55	62	46

tained relief simply by touching a drop of whisky to the tongue. A third patient (M.L.) thought that whisky relieved the sense of weakness that he ordinarily experienced after an attack. The fourth patient (E.B.) reported that whisky had previously

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## ALCOHOL IN THE TREATMENT OF ANGINA PECTORIS\*

SAMUEL STEARNS, M D,† JOSEPH E F RISEMAN, M D,‡ AND WILLIAM GRAY, M D §

BOSTON

THE earliest description of angina pectoris, that of Heberden<sup>1</sup> in 1786, refers to "the relief afforded by wine and spirituous cordials." Since then alcoholic beverages have frequently been recommended or at least permitted in the treatment of angina pectoris, but few efforts to evaluate such therapy have appeared in the literature. The present study was carried out to obtain an objective evaluation of the use of alcohol in the treatment of angina pectoris.

### SUMMARY OF THE LITERATURE

The comparative value of brandy, carminatives and nitroglycerin in the treatment of attacks of angina pectoris was studied in 1934 by Evans and Hoyle.<sup>2</sup> Patients kept a record of two-week periods, noting the number of attacks, the duration of pain and the effect of medication. Nitroglycerin was followed by great or moderate relief in 59 per cent of the cases. Approximately half the patients reported a similar result with brandy or carminatives. Objectively, 1 of 11 patients was able to do more work following the prophylactic use of brandy.

White,<sup>3</sup> without advancing statistical or experimental evidence, has named alcohol as the most effective drug, next to nitrates, in the treatment of angina pectoris.

The drinking habits of 750 patients with angina pectoris and of a control group have been reviewed by White and Sharber.<sup>4</sup> No significant differences were found in the percentages of nondrinkers and moderate drinkers in each group, there were, however, 67 patients among the controls who drank to excess, compared to 9 excessive drinkers with angina pectoris. One of the latter had survived for twenty-four years following the onset of angina pectoris, despite a daily intake of 1 quart of whisky. It was concluded that although alcohol neither caused nor prevented angina pectoris, excessive

drinking was rare in the past history of patients with this disease and that in occasional cases alcohol might prevent or relieve attacks.

Levy<sup>5</sup> also noted that the longest-lived of a large group of patients with angina pectoris was also the heaviest drinker.

### MATERIALS AND METHODS

Observations were made on 19 men and 2 women, aged thirty-nine to seventy-five years, with angina pectoris of six months' to fifteen years' duration. None were in congestive failure, and only 1 had had a recent cardiac infarction. Of 11 patients in whom a history of the use of alcoholic beverages was recorded, 2 were total abstainers and 9 were infrequent or moderate drinkers. The heaviest drinker used not more than 2 or 3 ounces of whisky on any one day.

Each patient had been a regular weekly visitor to the Angina Pectoris Clinic of the Beth Israel Hospital for four months to thirteen years, during which time the objective response to a wide variety of medications, including nitroglycerin, had been repeatedly determined.<sup>6,7</sup> Six patients showed a marked response to medication, 7 a moderate response, and 8 little or no response. The patients were therefore classified as belonging to Group 1, Group 2 and Group 3, respectively, according to the criteria previously described.<sup>7</sup>

At each visit, patients were questioned concerning the number of attacks of angina, the number of nitroglycerin tablets used and the amount of physical and emotional stress experienced during the previous week. The patients' ability to work was then determined by the Standardized Exercise-Tolerance Test,<sup>8</sup> which consists of continuously ascending and descending a two-step staircase in a cold room (about 50°F) until angina develops. Only one test was performed on a given day, and no test was done if the patient had taken nitroglycerin in the preceding two hours. During the period of the tests with alcohol, patients received only placebo or other ineffective medication.

The following observations were made. In 8 patients, the comparative duration of induced attacks of angina pectoris when the patients were

\*From the Medical Service and Medical Research Laboratories, Beth Israel Hospital, the Department of Medicine, Harvard Medical School, and the Department of Medicine, Tufts College Medical School.

†Assistant in medicine, Tufts College Medical School; assistant in medicine, Beth Israel Hospital.

‡Associate in medicine, Harvard Medical School; instructor in medicine, Tufts College Medical School; associate visiting physician, Beth Israel Hospital.

§Assistant in medicine, Harvard Medical School; teaching fellow, Tufts College Medical School; medical resident, Beth Israel Hospital.

concentration of alcohol does not accumulate in the blood stream in this time, any clinical response following the drinking of 1 ounce of whisky is probably due to a reflex or psychogenic effect. That alcohol does exert a reflex effect on the cardiovascular system has been shown by many studies. Brooks<sup>9</sup> observed that 10 cc of 50 per cent alcohol introduced into the mouth of an unanesthetized dog resulted in an immediate sharp rise in blood pressure, whereas much larger doses given through a gastric fistula had no immediate effect. Lieb<sup>10</sup> found that in man a drink of 5 cc of undiluted whisky produced a small rise in blood pressure within one minute. Dixon<sup>11</sup> observed that the pulse was transiently accelerated by taking into the mouth whisky, mustard, hot water or other stimulants of the mucous membrane. Subsequently it was demonstrated by Grollman<sup>12</sup> that a dose of 15 cc of alcohol produced in nondrinkers a transient rise in pulse, blood pressure and cardiac output within ten minutes of ingestion. He attributed these effects to stimulation of vasomotor centers by afferent impulses arising in the mouth, pharynx and esophagus.

In the present study, such reflex mechanisms were not of therapeutic importance, for angina pectoris was neither prevented nor decreased in duration by exercising the patient with whisky held in the mouth.

#### *Vasodilator Mechanism*

The vasodilating effect of alcohol on cutaneous vessels is well illustrated by the flushing and sweating that follow the taking of whisky. This effect has been shown experimentally to occur following the absorption of alcohol. Lieb,<sup>10</sup> for example, showed that well diluted whisky had no cardiovascular effect until sufficient time for absorption had elapsed. Grollman<sup>12</sup> observed a rise in blood pressure, pulse and cardiac output in habitual drinkers as well as in nondrinkers within fifteen to thirty-five minutes after the ingestion of 35 cc or more of alcohol. This he considered to be compensatory to the cutaneous vasodilatation that would otherwise have resulted in a fall in blood pressure.<sup>12</sup>

Although a coronary vasodilating action has been assumed for alcohol,<sup>14</sup> there is little experimental evidence that this occurs. Dixon<sup>11</sup> found that perfusion of an isolated segment of the coronary artery of a rabbit with 0.1 to 0.2 per cent alcohol in saline solution caused extremely slight vasodilatation. Sulzer<sup>15</sup> observed that the first noticeable effect of alcohol on the coronary flow of a dog heart-lung preparation was invariably a decrease. An increase in concentration of alcohol from 0.13 to 0.21 per cent produced a further decrease of 17 per cent in coronary flow. Gilbert and Fenn<sup>16</sup> found that the slow intravenous injection of 0.3 cc of 80 per cent alcohol per kilogram of body weight

into the intact dog caused no increase in coronary blood flow, although increases of up to 50 per cent were obtained following the use of various theobromine derivatives. Such concentrations of alcohol approximate the intoxication level in man<sup>17</sup> and are not produced by ordinary therapeutic doses.

In the present study, any coronary vasodilatation that may have occurred was not of therapeutic value.

#### *Central-Nervous-System Mechanism*

Pharmacologists teach that although ethyl alcohol superficially appears to produce stimulation, it is actually a depressant of the central nervous system.<sup>14</sup> It has been stated that blood concentrations considerably lower than those associated with clinical intoxication may impair the function of the higher centers in man.<sup>17</sup> By this mechanism alcohol is probably capable of producing the observed effects of decreasing anxiety, diminishing attention to pain and promoting a sense of well-being.<sup>18</sup>

Regardless of its physiologic effect, the psychogenic effect, real or imaginary, has been commented on by many clinicians, including Osler<sup>19</sup> and Brooks.<sup>20</sup>

In this study, 7 of 9 patients who drank 1 ounce of whisky four times daily for one week reported subjective improvement. Two of these had no attacks of angina during the week of treatment. Objectively, one of them showed a 23 per cent increase in ability to exercise and another a 33 per cent decrease. The remaining 5 were able to do no more work under standardized conditions. Since similar results—that is, subjective without objective improvement—were noted in patients treated by multiple small doses of opiates or barbiturates,<sup>21</sup> it is not improbable that alcohol is also capable of decreasing attention to pain or of increasing the threshold of awareness of pain. Two patients were made subjectively worse, one stopping the medication because of the increased severity and frequency of anginal attacks. The mechanism of such unfavorable reactions is not obvious.

Judging from the literature, it is difficult to evaluate the effect of alcohol. In the present study, an attempt was made to measure objectively the clinical effect of alcohol in angina pectoris. Although no increase in ability to work resulted from this type of therapy and no decrease in the duration of an attack of angina pectoris occurred in the majority of patients, alcohol nevertheless seems capable in some cases of producing a certain type of subjective comfort. This may be of some value in the general management of the patient with angina pectoris. It is doubtful whether such medication has a specific effect on the course or severity of the disease.

#### CONCLUSIONS

Therapeutic doses of whisky do not measurably shorten the duration of attacks of angina pectoris or increase the capacity of the patient with angina for work.

decreased the severity of attacks if taken when pain was coming on, in recent years this effect had not been obtained. All 5 patients used nitroglycerin as the drug of choice for the treatment of attacks.

### *Effect of Single Doses of Alcohol on Ability to Exercise*

Of the 21 patients who took 1 ounce of whisky up to ninety minutes before performing the Standardized Exercise-Tolerance Test, 5 were able to do from 18 to 27 per cent more work than was otherwise possible (Table 2). These increases in exercise tolerance occurred thirty, sixty and ninety minutes after the ingestion of whisky by

ardized Exercise-Tolerance Test, 2 (N S and E B) had no attacks of cardiac pain during the week. This result was not associated with any change in exercise tolerance. Five patients felt subjectively better while on regular doses of whisky. One patient (S L) showed a 23 per cent increase in exercise tolerance, another (H B) showed a 33 per cent decrease, and 3 (B K, E B, and S W) showed no change. The eighth and ninth patients of the group (R S and S R) experienced increased frequency and severity of angina, and 1 patient (R S) was forced to discontinue the medication after several days because of ten to twenty attacks of

TABLE 2 *Effect of Whisky on Ability to Work as Measured by Standardized Exercise-Tolerance Test (in Trips)*

Test (in Trips)												
NAME	SEX	USUAL RANGE WITH NO THERAPY	2 MINUTES AFTER TAKING 0.3 MG OF NITROGLYCERIN	MINUTES AFTER DRINKING 1 OZ OF WHISKY							1 OZ. OF WHISKY 4 TIMES DAILY FOR 1 WEEK	1/2 OZ. OF WHISKY IN MOUTH
Group 1				0	5	10	15	30	60	90		
S.R.	M	24-30										
E.A.	M	25-30	51	24	28	34	30	36	37	38	22	30
H.S.I.	M	35-44	90	26*			26*					
H.St.	M	30-38	77	46*	44*		55*					
E.B.	M	18-24	72		45*							
I.B.	M	38-49	38	21	17	24	26	24	21		22	20
			113		50		50					
Group 2												
N.S.	M	18-22										
H.B.	M	33-40	34	19	16		22	24	26	20	22	20
M.L.	M	38-46	64		38	48	51					
L.G.	M	21-26	56	42	46	42	42	36	38	36	27	34
I.F.	M	55-65					23*					
S.W.	M	25-32	88	49	55		70					
R.R.	F	20-24	50		24							
			31†	22	24	18	17		22		26	31
											24†	22
Group 3												
S.L.	M	27-31	34†		32	34		26	31		38	
R.S.	M	22-28	30	24	24	28	28	27	28		26	20
B.K.	F	24-30	34	18	18	30	16	30	36		26	
M.P.	M	30-35	35	34*	35*							
J.G.	M	9-12	10	14			31*					
B.F.	M	24-26		20*	24*							
B.A.	M	31-38	41	29*	31*			24*				
R.K.	M	8-15	16		14		43*	11	15			17
*50 per cent alcohol used in place of whisky												

\*50 per cent alcohol used in place of whisky

†No cardiac pain. Exercise stopped because of fatigue.

one patient (S R), ten, thirty and sixty minutes after taking whisky in another (B K), and between five and fifteen minutes after taking whisky in the remaining 3 (H St, H Sc and H B).

In similar determinations, with 0.3 mg of nitroglycerin taken two minutes before exercise, 4 of these 5 patients were able to do 60 to 75 per cent more work than usual. The fifth patient (B K) could do only 13 per cent more work than usual.

Of the 16 patients who showed no response to alcohol, 3 patients (Group 1) did 60 to 200 per cent more work after nitroglycerin, 5 patients (Group 2) showed 21 to 56 per cent increases after nitroglycerin, and 7 patients (Group 3) did not respond to nitroglycerin.

### *Effect of Multiple Doses of Alcohol on Ability to Exercise*

Of the 9 patients who drank 1 ounce of whisky four times daily for one week, together with a final dose immediately before performing the Stand-

chest pain daily instead of the usual two or three. When whisky was discontinued, the attacks promptly decreased to their usual frequency.

### *Effect of Alcohol Held in the Mouth on Ability to Exercise*

The experience of 1 patient (R S) that touching a drop of whisky to the tongue relieved his anginal attacks was tested in this patient and 7 others. No patient showed an increase in ability to work or a change in the nature of anginal pain when exercising with 1/2 ounce of whisky held in the mouth.

### DISCUSSION

According to the literature, alcohol may affect the patient with angina pectoris by a reflex or vasodilator mechanism or through the central nervous system.

### *Reflex Mechanism*

Almost all attacks of angina pectoris are of less than three minutes' duration.<sup>8</sup> Since a significant

ture and should establish diagnosis before serious shock results

The treatment must be dictated by the circumstances of the case. Transfusions, operation for ligation of the vessel if bleeding seems to be continuing, the giving of blood coagulants, tight compression and, if necessary, termination of pregnancy are indicated. Termination by cesarean section must be seriously considered if the patient is at term, with a live baby, and not in labor. Since labor strain in itself has been a cause of hematoma, it seems unwise to subject a patient to operation for ligation of the bleeding vessel and within hours or a few days to have her undergo labor, with its additional strain on a damaged rectus abdominis muscle and potential resumption of bleeding. In a multipara not at term, operation for ligation of the bleeding vessel may be sufficient.

If active bleeding has ceased, emptying of the hematoma is neither necessary nor wise, since removal of the clot decreases the pressure on the bleeder and may reactivate the bleeding. Prevention of breakdown and infection may be accomplished by the use of regional and systemic penicillin therapy. If hemorrhage is still in progress, ligation of the offending vessel must be attempted.

### CASE REPORT

M. H., a 36-year-old, married tripara, began her last regular period on February 13, 1945, and the expected date of the confinement was November 20. The two previous pregnancies had been successfully terminated by low-forceps deliveries of living normal babies. The past history was negative. There had been no operations.

The prenatal period followed an even, uneventful course. The blood pressure vacillated between 118/62 and 126/70. The urine was consistently normal, and there were no signs or symptoms of toxicity. In the 3rd month, the red-cell count was 4,250,000, the hemoglobin 82 per cent, and the white-cell count 8200. A blood Hinton test was negative. The blood was of Type A and was Rh+. Quickening was noted in the 4th month, and fetal activity continued throughout the pregnancy.

One week before term, the patient had an acute upper respiratory infection with an associated tracheobronchitis. On November 23, a complaint of severe left-sided abdominal pain, associated with nausea and vomiting of 3 hours' duration, was made by telephone. Examination at the patient's home revealed a woman in moderate distress, walking about and holding on to the left side of the abdomen. The pulse was 78 and of good quality. The temperature was 98.4°F, and the blood pressure 120/68. The skin was moist and of normal color. The abdomen was nontender and revealed a uterus at term. A vertex presented and was lightly engaged. The position was O.L.A., and the fetal heart, heard in the left lower quadrant, was of good quality, with a rate of 132. The fetus seemed of normal size. Adjacent to the left cornu was a small, rounded mass the size of a lemon. It was tender and the tenderness was transmitted to the left lower quadrant. There was no muscle spasm or rebound tenderness. Both flanks and costovertebral angles were negative. There was no vaginal bleeding or discharge. The bowels had been sluggish for the last 24 hours. On the previous day the patient had had severe, sustained spasms of coughing which were so intense that she had not felt like eating. During the night there was left-sided pain and nausea.

Three hours after this examination, the pain became so severe that the patient was admitted to Wyman House Cambridge Hospital, for observation. The temperature was 97.4°F, the pulse 104, and the blood pressure 102/60. The red-cell count was 3,640,000, the hemoglobin 75 per cent,

and the white-cell count 15,400. A catheter urine specimen was negative except for occasional white and red cells. The abdomen revealed a mass along the left side of the uterus. It was firm and rounded at the top and the size of a small grapefruit, and extended indefinitely downward. It was exquisitely tender. There was slight muscle spasm, but no rebound tenderness. Rectal and vaginal examinations were negative. The fetal heart beat was present in the left lower quadrant of the abdomen and was of good quality and rate. Fetal motility was palpable and visible. The skin was somewhat pale. No cyst or fibroid had ever been palpable on previous examinations. A provisional diagnosis of ovarian cyst with a twisted pedicle and hemorrhage was made, and a consultant concurred in it. Cesarean section and exploratory laparotomy were decided on.

Under spinal anesthesia, a midline incision was made through the skin and fat. The anterior fascia appeared normal and was incised. The underlying muscle and posterior fascia were cyanotic and edematous. The peritoneum was slightly blue. When the peritoneum was incised, the abdominal cavity was found to be normal. Palpation of the abdominal wall through the incision revealed a mass that started 2 fingerbreadths below the left costal margin and extended downward. It was round and measured 10 cm in diameter and 5 cm in thickness. This was obviously a large hematoma in the left rectus muscle, with extravasation of blood down through the muscle almost to the crest of the ilium. In view of this and the probable result of labor, which was imminent, being 3 days overdue, it was deemed advisable to terminate the pregnancy by cesarean section. A longitudinal cervical section was performed, and a living female baby was readily extracted. Two grams of sulfanilamide powder was dusted over the uterine incision before the bladder reflex was sutured over. The hematoma was more carefully examined, and it was decided that emptying it would be unwise, since the release of tension might result in resumption of active bleeding. Any attempt to dissect above the hematoma to find the bleeder was likewise considered unwise. To aid in prevention of breakdown and secondary infection of the hematoma, a dose of 100,000 units of penicillin sodium in 5 cc. of normal saline solution was injected into the hematoma by means of a long needle traversing the rectus muscle. The abdomen was closed in layers without drainage or retention sutures. The patient was returned to bed in good condition, and the indwelling Foley catheter was connected to a drainage bottle. Penicillin was injected intramuscularly in doses of 20,000 units every three hours for the next 3 days.

The postoperative course was uneventful. Within 24 hours the hematoma was appreciably smaller, and it continued to decrease in size until at discharge 2 weeks after operation it was barely palpable. The wound healed by first intention. The mother and baby were discharged in good condition.

### SUMMARY

Hematoma of the rectus abdominis muscle may occur during pregnancy as the result of coughing.

The diagnosis is often missed because of the lack of awareness of such an entity.

The mortality in reported cases is high but can be made much lower.

Early diagnosis and operation, with cesarean section if the pregnancy is at term, offers the best opportunity for obtaining a live mother and baby.

A typical case, with recovery, is reported.

483 Beacon Street

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In many patients with angina pectoris, whisky may promote an increased sense of well-being without associated objective improvement. A few patients, however, are made subjectively worse.

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## SPONTANEOUS HEMATOMA OF THE ABDOMINAL WALL IN PREGNANCY

### Report of a Case

DAVID ROSE, M.D.\*

BOSTON

THE occurrence of spontaneous hematoma of the abdominal wall in pregnancy is relatively rare. Perusal of the literature reveals a complication of 28 cases by Torpin.<sup>1</sup> Thomas<sup>2</sup> reported an additional case that involved a full-term pregnancy, with a resultant live mother and a dead baby. Cesarean section was performed after the patient had gone into shock. Dawson<sup>3</sup> reported the occurrence of hematoma in a full-term pregnancy. Cesarean section was performed and a live baby was delivered. Liggett<sup>4</sup> reported a case in a sextipara at seven months in which he operated and ligated the ruptured blood vessel. Two months later a live baby was delivered from below. This brings the total of reported cases, exclusive of the present one, to 31.

Spontaneous hematoma is the result of rupture of the main inferior epigastric artery or one of its branches. In the 31 cases in the literature, the left-side and right-side occurrences were about equal in number. Almost all the patients were multiparas of thirty years of age or older. In 18 cases, cough was the causative factor. The cause in the remainder was the strain of labor or extraneous factors. The hematoma occurred at term in 9 cases and in the last trimester of pregnancy in 12.

The most striking feature in the reported cases was the high maternal and fetal mortality. Torpin gave a maternal mortality of 15 per cent. There were no maternal deaths in the other cases, so that

the over-all mortality was 13 per cent. The fetal mortality in Torpin's review was also 15 per cent and the fetal death in Thomas's case makes the over-all mortality 16 per cent.

The percentage of maternal and fetal deaths is sufficiently high to merit serious consideration of this condition as a definite hazard, to be included with the other serious hemorrhages found in the later stages of pregnancy. Early recognition and appropriate treatment will definitely decrease the mortality rate, since almost all the reported deaths resulted from hemorrhage continuing to the point of severe shock.

The diagnosis of hematoma can be easily made if one remembers that such a condition can occur. In the case reported herein, the diagnosis was missed because the possibility of such an occurrence was not entertained. It was this fact, together with the similar mistake in diagnosis that prevailed in most of the other cases, that prompted the writing of this paper. The wider dissemination of knowledge that rupture of a vessel of the abdominal wall, with resultant hematoma, into the rectus abdominis muscle can and does occur during pregnancy will doubtless make for more accurate diagnoses, more efficient treatment and a lessened mortality. The appearance of a tender abdominal tumor that increases in size, with a history of cough, should make one aware of the possible hematoma. Continuing observation, with blood studies, x-ray examination and even diagnostic needling of the tumor, coupled with signs of concealed bleeding, completes the pic-

\*Associate surgeon, Cambridge Hospital; senior visiting surgeon, Cahill House, Cambridge City Hospital.

In general, spontaneous variations in blood flow were more frequent the higher the water temperature.

At least five factors influenced the deep-muscle temperature—the water-bath or environmental temperature, the length of the exposure, the rate of blood flow, the body temperature and the local metabolic rate. In water baths below 35°C attainment of a steady deep-muscle temperature required an hour or more, in baths at 13°C, it required about two hours. At bath temperatures above the body temperature, equilibrium was reached within one hour. The steady deep-muscle temperature was 4 or 5° higher than that of a water bath at 13°C, and about 2.5° above baths at 20 to 32°C. The rapid initial fall in baths below 20°C was due to the greatly decreased blood flow. When the water-bath temperature equaled the body temperature, the deep-muscle temperature was about the same. At higher bath temperatures the rise in deep-muscle temperature decreased progressively with each increase in bath temperature, and at bath temperatures of 42.5 and 45°C the deep-muscle temperature was usually 39°C. In some cases, however, the deep-muscle temperature diminished when the bath temperature was raised from 42.5 to 45°C, because of the greatly increased blood flow at the higher temperature. In cold baths, those at 13°C, the sensation of cold lasted for only ten minutes. There was no discomfort, but when the arm was taken out after two hours or more, muscular movements were difficult and slow. There was no generalized shivering. Immersion of the forearm in warm baths caused a small, sharp rise in body temperature as the large volume of blood flowing through the arm was heated, this was followed by a plateau and a fall. The body temperature, however, differed by only about 1°C from that of the arm in the coldest and hottest baths employed. Barcroft and Edholm point out that the increased blood flow through the arm at high temperatures almost certainly involved vessels in the muscles as well as in the skin.

Paralysis of the sympathetic supply of the right arm by novocain, given by the paravertebral route, caused the same increase in blood flow in the right hand as did immersion in water at 43°C.<sup>5</sup> It thus appeared that inhibition of sympathetic activity could account for full vasodilatation in the hand and that there was no need to assume that the sympathetic nerves running to the hand contain vasodilator fibers. Similar evidence was provided for the absence of vasodilator fibers in the sympathetic nerves running to vessels in the forearm.

Peripheral vasodilatation or vasoconstriction produced by warming or cooling the body caused only minor changes in cardiac output. This was attributed to the buffering capacities of the vasomotor system.<sup>6</sup>

The increase in local circulation rate and augmented capillary pressure increased the rate of

edema formation when venous pressure was maintained, so that there was expected to be an increase in lymphatic drainage. In the presence of some lymphatic blockage, however, low-grade subclinical edema might be produced. Warmth was shown to increase the lymphatic capillary network and lymph formation. These changes occurred particularly at temperatures between 45 and 50°C in experiments on cervical lymph flow. At about 50°C, however, changes in capillary permeability that were not immediately reversible occurred.<sup>7</sup>

**Blood.** Bazett<sup>8</sup> has stated that a rising blood temperature particularly affects the dissociation constants of acid radicals of proteins, with the result that proteins combine with base that was previously in the form of sodium or potassium bicarbonate. The carbon dioxide thus freed greatly increases acidity and carbon dioxide tension. An alteration of 10°C (18°F) causes an increase in acidity comparable to the normal difference between arterial and venous blood. It is possible that these changes in acidity and gas tension are of some importance in modifying the reactions of tissues to infection. The activities of leukocytes in phagocytosis are probably also modified, since in vitro experiments show maximal velocity at 40°C. Studies by Spangenberg,<sup>9</sup> however, on the effect of external applications of thermal agents on inflammatory reactions in the rabbit showed no significant changes in the cytologic response.

**Metabolism.** It is well known that increase in temperature has a definite effect on metabolic changes in any tissue, such that the speed of chemical reactions is increased two or three times with a rise of 10°C. This is of considerable clinical significance when heat is applied to the extremities of patients suffering from obstructive arterial disease. In such cases the increase in the metabolic rate and consequent oxygen consumption produced by local exposure to heat may exceed the possible reflex increase in arterial supply. The net result is a relative diminution in the supply of oxygen as compared to the augmented need subsequent to temperature increases. For studies on the influence of temperature on oxygen consumption, the reader is referred to the review of Field and Hall.<sup>3</sup>

**Nervous system.** Local application of heat is known to influence the sympathetic nervous system. Gibbon and Landis<sup>10</sup> have observed that immersing the upper extremities in warm water produces vasodilatation in the lower extremities. External applications are also found to affect the transmission of painful stimuli. Although in some experiments the counterirritation thus produced lessens the recorded potentials in sensory nerves, the complete mechanism of effectiveness is not known. The impression was gained from similar studies by Gammon and Starr<sup>11</sup> that intermittent application of heat and cold was more effective than either agent used alone. Other experimental studies

## MEDICAL PROGRESS

### RESEARCH IN PHYSICAL MEDICINE

ARTHUR L. WATKINS, M.D.\*

BOSTON

**E**VALUATION of any therapeutic agent, including physical therapy, must be gauged by its effect on patients and based on knowledge of physiologic action. Scientific investigation in the field of physical medicine is difficult because of the wide variety of agents employed—massage, therapeutic exercise, water, air, radiations (heat, light and ultraviolet rays), vibrations (mechanical and sound) and electricity in various forms. The conditions treated are often ill defined regarding etiology and pathology, and prescription of physical therapy is consequently often empirical, with hope entertained for symptomatic relief. In spite of these well known shortcomings, there is some background of known biologic effects of such physical agents, based on scientific research, which should be recognized by all physicians who prescribe physical therapy. Since instruction in this subject is largely omitted in medical-school curriculums, it seems worth while to review the scientific basis of physical medicine for the benefit of the practicing physician.

#### HEAT AND COLD THERAPY

##### *Physiologic Effects of Heat*

The external application of heat has been used almost instinctively for centuries by sick and injured men and animals. The present knowledge of the actual effects of heat is based on data obtained rather recently. Heat is received in the form of radiant energy, more or less constantly from exposure to sunlight and occasionally from artificial sources. In considering the action of radiant energy it is customary to classify it in subdivisions according to wave length. Beginning with the shortest wave lengths, there are ultraviolet light (180–390 millimicrons), visible light (390–760 millimicrons), near infrared light (760–1500 millimicrons), intermediate infrared light (1500–3000 millimicrons) and far infrared light, with wave lengths greater than 3000 millimicrons. Since the effect of ultraviolet and visible energy is not primarily thermal, these wave lengths will be considered later.

The infrared, or heat, rays employed for therapeutic purposes are generally divided according to their power to penetrate the skin. Heat from nonluminous sources, such as hot-water bottles, hot packs and hot-water baths, does not penetrate the skin more than 1 millimeter, and heating is

effected only by conduction. Energy from luminous sources of heat, however, such as sunlight and tungsten-filament and carbon-filament lamps, is transmitted through the outer layers of the skin, and some slight depth effects are possible.

The rate at which changes of temperature penetrate the tissues is slow, for heat capacity is high and large quantities of heat have to be transported before the temperature of the tissues is greatly altered. Although the temperature of the tissues can be raised to 37°C (98.6°F) with relative rapidity, beyond this point, through the action of circulatory reflexes, heat is quickly dissipated, provided the circulation is intact.<sup>1</sup>

*Circulation.* An outstanding effect of local exposure to heat is stimulation of the vasomotor reflexes.<sup>2</sup> When following local exposure to heat the temperature of a part is increased from 18 to 39°C, the number of open capillaries is increased, tissue metabolism is accelerated, and the rate of exchange between blood and tissues is increased. Above this temperature the number of open capillaries is greatly increased, and the rate of blood flow is so rapid that the blood entering the veins simulates arterial blood and contains 91 per cent of its saturated value of oxygen, as compared with the usual value of 70 per cent, provided the circulatory system is not diseased. Local heating therefore produces peripheral vasodilatation, raises capillary blood pressure and through relaxation of capillaries increases the area of capillary wall available for fluid interchange.

Recently Field and Hall<sup>3</sup> have reviewed over a hundred articles on the physiologic effects of heat and cold, written in the last three years. A paper of particular clinical interest, by Barcroft and Edholm,<sup>4</sup> deals with the influence of water-bath temperatures ranging from 13 to 45°C on blood flow and deep-muscle temperature in the human forearm. Flow-time relations were considered with reference to three temperature ranges—13 to 35°C, 37 to 42.5°C and 45°C. At temperatures of 13 to 35°C, the flow remained quite constant after the first fifteen minutes. At 37 to 42.5°C it rose to a maximum in periods that shortened as the external temperature rose. Progressive diminution followed this peak, so that no steady state was attained. Factors possibly contributing to this effect are discussed. At 45°C, the blood flow rose to a maximum in about thirty minutes and remained at this high level or even slightly increased.

\*Associate in medicine, Harvard Medical School, chief of physical medicine, Massachusetts General Hospital.



to those observed following the fatal administration of nitrous oxide anesthesia. In some cases sudden death during hyperpyrexia has been caused by extensive hemorrhage into the endocardium of the left ventricle and into the septal wall in the region of the bundle of His.

Experiments have shown that *Neisseria gonorrhoeae* is generally destroyed in six to twenty-seven hours by a temperature of  $\pm 1$  to  $\pm 1.6^{\circ}\text{C}$ . Although in these bacteria may be destroyed by the production of fevers in this range, artificial fevers are generally thought to be effective through improvement with bodily defense rather than through destruction by heat alone.

**Clinical applications** After many years of clinical and laboratory experiments, safe procedures for the induction of artificial fever have been established. These are described in the standard textbooks of physical medicine. Several methods of heating are satisfactory, since they all are based on the fundamental principle of preventing heat loss by an insulated cabinet and transferring heat by conduction from circulating hot air to the body or by conversion of high-frequency electrical energy by means of short-wave diathermy. It has been emphasized that production of fever by physical means is strictly a hospital procedure, to be carried out only by well trained personnel. Experience has shown that patients should be selected with as much care as are those who are to undergo major surgical operations. The chief usefulness of artificial fever lies in the treatment of gonorrhea, both acute and chronic, and its complications and in that of syphilis. Fever therapy is occasionally valuable for treating intractable bronchial asthma, chorea and undulant fever.

#### *Physiologic Effects of Cold*

Great interest in the effects of cold and numerous studies on the subject have followed the pioneer work of Smith and Fay<sup>25</sup> in the treatment of cancer with temperatures maintained at levels of 75 to 90°F. Studies at these temperatures have shown that the circulatory rates of blood flow are markedly lessened and blood pressure is decreased.<sup>26</sup> Electrocardiograms reveal irregularities and changes in the QRS complex and ST intervals. Blood-chemical changes are minimal. Undifferentiated cell growth, such as occurs in cancer, has been found to require an optimal critical temperature level below which degenerative changes occur, whereas normal cellular tissue is capable of withstanding temperatures between 90 and 95°F or lower. On this basis, patients with inoperable cancer have been given hypothermia, with some temporary good results. Relief of pain has been noted in terminal states of metastatic cancer following hypothermia. Other neurologic changes have included an increase in the deep reflexes in moderately low temperatures and absent reflexes as the temperature approaches

78°F. The pupillary reflexes are also altered, dysarthria has been observed, and there is delayed cerebration, including retrograde amnesia. In schizophrenic patients marked changes in mental status have been seen.<sup>27</sup> Although regressive changes in cancerous tissues have been noted, cures have not been obtained.

Short exposures to cold also have definite effects. A cold bath, for example, produces the well known changes in the skin described as "gooseflesh," with diminution of capillary blood flow and obvious pallor. Following this there is a reactive hyperemia, with dilatation of the cutaneous vessels. The effects on the circulation rate vary in different subjects. Respiratory action is increased by short applications of cold and later becomes regular and deep. The metabolic rate is usually elevated from the shivering induced. Locally the metabolism is decreased in areas in which there is vasoconstriction of all surface vessels including arteries, arterioles, capillaries, venules and veins. Alterations in temperature are greater with cold than with heat applied locally, so that cold is often said to penetrate better. One of the most important effects of cold is through its sedative action on the nervous system. Mild applications may be used for relief of pain, and actual refrigeration has been found to be an effective anesthetic agent for surgery.<sup>28</sup> Wound healing has not been interfered with in these cases.

#### LIGHT THERAPY

There is a general belief in the therapeutic value of sunlight. Although it is well known that sunlight is necessary and beneficial for plant life, the analogy that it has widespread therapeutic value for man is lacking in scientific proof. Whereas, strictly speaking, light refers only to the wave lengths that produce visual sensation, it is the usual practice to include the invisible ultraviolet rays in discussions of light therapy. The invisible infrared rays have already been considered under the subject of heat. Knowledge of the effect of sunlight, particularly visible and ultraviolet rays, in relation to disease processes is somewhat scanty, but there is a large body of literature based on physical studies in relation to cellular activity and chemical processes. Effects of ultraviolet radiation and sunlight that are of particular interest in relation to medicine have been recently reviewed by Blum.<sup>29</sup>

#### *Physical Aspects*

Some of the established facts concerning penetration and absorption are of interest and will accordingly be briefly summarized. Transmission is extremely low for wave lengths shorter than 320 millimicrons, the spectral region of ultraviolet radiation that is of biological interest. Such radiation is largely absorbed in the epidermis, principally by protein. Transmission increases progressively

have been made on the influence of thermal agents on gastric and intestinal motor activity. Bisgard and Nye<sup>12</sup> found that heat applied to the abdominal wall inhibited motor activity in the stomach, small bowel and colon. Heat applied directly to the stomach from drinking warm liquids, however, had the exactly opposite effect. The conclusions from these studies were that to inhibit the motor activity in the gastrointestinal tract in the presence of inflammatory lesions, such as appendicitis, hot applications rather than cold are indicated.

Recently the effect of heat on skeletal muscle has also been studied particularly in relation to poliomyelitis. During the acute stages of this disease muscles are found to be abnormally sensitive to passive stretching, as indicated by electromyography<sup>13, 14</sup>. Heat, particularly in the form of luminous radiation, diminishes this spasm or hyperirritability<sup>15</sup>. Other studies have shown that heat influences the relaxation phase of muscle contraction<sup>16</sup> but that strength is not improved by application of hot packs<sup>17</sup>.

*Temperature sensation.* Oppel and Hardy<sup>18</sup> have studied the response of the skin to sunlight, visible light and infrared radiation. The infrared rays are divided into those of wave lengths shorter than 3000 millimicrons, designated as penetrating rays, and those of longer wave lengths, designated as nonpenetrating. These authors studied the stimulating effect on sensation of visible light and of penetrating and nonpenetrating infrared radiation and found that the more penetrating the rays, the less sensitive was the subject to them. The skin-surface temperature was elevated highest by nonpenetrating radiation and least by visible light. Hardy and Oppel<sup>19</sup> found that the smallest rate of radiation that the body is capable of receiving as warmth is 0.00015 gram-calorie per centimeter<sup>2</sup> per second. This amounts to one nine-millionth of the normal hourly loss of radiation from the body surface. The intensity of stimulus necessary to evoke sensation increases as the area stimulated is decreased, although in all cases the magnitude of the stimulus required decreases as the area exposed decreases. These authors' method of measuring the pain threshold has proved to be of some clinical value in evaluating patients' sensitivity to pain and in judging the effectiveness of analgesic drugs in the alleviation of pain.

#### *Local Application of Heat*

Few experimental data are available that will help the physician to determine the accurate and optimum dosage of thermal agents. Some studies<sup>20</sup> have been made on changes in skin temperature with different sources of heat at different distances. In general these show that penetrating, infrared radiation is more efficient than the nonpenetrating type or other sources of heat whose transport is largely effected by conduction. It is also known

that effective heating cannot be produced by the usual clinical methods in less than thirty to forty-five minutes. Although some experimental devices for measuring radiant heat have been produced,<sup>21</sup> dosage is still gauged chiefly by the comfort of the patient, and the duration of treatment is too often determined more by habit and convenience than by knowledge of physiologic effects.

#### *General Application of Heat (Fever Therapy)*

Much of the present knowledge concerning the effects of heat has resulted from numerous scientific studies on artificial-fever therapy. Over six hundred articles on this subject have been written, and many scientific facts have been established and recently summarized in reviews<sup>22-24</sup>.

*Physiologic effects.* Increases in the pulse and the circulatory rate, resulting in a greater volume output of the heart, are outstanding. The maximal increase of circulation occurs between temperatures of 103 and 104°F. Electrocardiographic changes show decreased conduction time and irregularities. The blood volume and viscosity are little altered provided the intake of fluids is sufficient. If there is severe sweating without replacement of fluids, however, the reduction in blood plasma may be sufficient to produce peripheral vascular collapse. Capillary hemorrhages may occur at levels of pressure rendered abnormally low by decreased capillary resistance.

Absorption of fluid from the intestinal tract is frequently retarded during fever therapy, making intravenous administration of fluids necessary. The red-cell count of the circulating blood is generally unchanged, but following an initial decrease the white-cell count rises to levels ranging from 10,000 to 60,000. This leukocytosis is greater in shorter and less intense sessions of fever. Prolonged fevers at high temperatures have been shown to lead to leukopenia. Toxic changes in the polymorphonuclear leukocytes are frequently noted. Artificial fever may produce thrombocytopenia and a decrease in prothrombin and fibrinogen following hepatic damage, so that coagulation of blood is interfered with, leading to potential or actual hemorrhage.

There is slight alteration in the chemical constitution of the blood, aside from changes in the acid-base equilibrium. Marked alkalosis may occur in fevers characterized by severe dehydration and hyperventilation. If no sodium chloride is administered and sweating is profuse, a diminution of chloride is to be expected. The basal metabolic rate is increased by approximately 7 per cent for each degree of fever induced.

Hemorrhagic encephalitis and hemorrhagic pneumonitis have been noted in some cases in which extreme hyperpyrexia has been induced. Adrenal hemorrhage and destruction have also been observed. Post-mortem findings have been similar

in the permeability of lymphatics, hyperesthesia and chemical changes, including enzyme activity

Pigmentation, or sun tanning, is associated with migration of melanin to the superficial layers of the epidermis. There is probably also some formation of new melanin, particularly by ultraviolet rays of greater wave lengths, which may explain the greater tanning effect of sunlight as compared with mercury-arc sources, which have little of the longer ultraviolet radiation.

The existence of tolerance or immunity to sunburn is well recognized. Although it is generally thought that sun tan explains tolerance to increasing exposure to the sun, recent observations have shown that this is not true. This evidence indicates a thickening of the corneum as the major factor in determining tolerance.

### *Practical Applications*

**Quantitative aspects** The usual measure of the effect of sunburn on the skin is the degree of erythema developed in response to a given dose of ultraviolet radiation. These effects, however, are subject to considerable uncertainty, owing to the number of variable factors influencing the erythema reaction. These include the transmissibility of the corneum in determining the amount of radiation reaching the living cell. The development of the erythema is known to vary in different persons, and the complex nature of the reaction itself makes measurement extremely difficult. Heating of the skin has been shown to shorten the time of appearance of the erythema but to have little effect on the erythema threshold. Sulfanilamide, on the other hand, lowers the threshold, and probably other drugs have similar effects. The erythema threshold varies considerably among different persons, and in the same persons from time to time and from one skin area to another. There is a widely held belief that there is a close relation between the type of complexion and susceptibility to sunburn, but exceptions to these rules are well known. The erythema threshold remains the best yardstick of dosage for clinical use, in the absence of any measuring device equal or superior to it.

**Cancer** There is strong evidence of a relation between ultraviolet radiation and human cutaneous cancer. In support of this concept are the facts that cancer of the skin occurs principally on the parts of the body most exposed to sunlight, is more frequent among outdoor than among indoor workers, is greatest in the regions of the earth receiving the greatest radiation and is less frequent in the Negro race than in the white race, and that cancer may be produced in the skin of laboratory animals by exposure to ultraviolet radiation.<sup>31</sup> The latter has also been shown to induce mutations in certain organisms.

**Vitamin D** Much of the propaganda concerning the beneficial effects of sunlight and ultraviolet

radiation is based on the only clear-cut beneficial effect known to be produced — namely, the formation of vitamin D and the resultant antirachitic action. It is now well known that vitamin D is formed by the action of ultraviolet rays of wave lengths shorter than approximately 320 millimicrons on 7-dehydrocholesterol or some closely similar precursor steroid compound. The photochemical reaction responsible for this process takes place near the surface of the skin, probably in the corneum. Further discussions of this subject may be found in any standard textbook of medicine or physical medicine.

**Photosensitization** Minor quantitative and qualitative variations in susceptibility to sunburn are well known. When these deviations are considerable, sensitivity is said to exist and may be induced by the presence of certain photosensitizers in the body. Among substances possessing photodynamic action may be mentioned various dyes and pigments, particularly porphyrin. A complete discussion of these rather rare conditions may be found in Blum's<sup>32</sup> book on the subject.

**Other effects** As knowledge concerning the cutaneous effects of sunlight accumulates, there is less evidence to credit numerous claims of widespread benefit. Wave lengths longer than 320 millimicrons have no specific photochemical effect other than pigment darkening, which extends through about 420 millimicrons. Wave lengths shorter than 320 millimicrons are known to have bactericidal action. Ultraviolet radiations of wave lengths that produce sunburn cause injury to the cells of the cornea and conjunctiva, resulting in a condition characterized by pain, visual disturbances, photophobia with excessive secretion, edema and purulent discharge. Such sunburn of the eye, however, does not confer protection against subsequent exposure. This condition also frequently results from exposure to artificial sources of radiation, particularly welding arcs. The damage to the eye from looking directly into the sun, as during an eclipse, is probably due to heating of the retina by infrared radiation rather than ultraviolet. The high incidence of cataract among glass blowers is also thought to be due to the infrared radiation rather than the ultraviolet.

In considering the systemic effects of sunlight, the solar heat load must be considered. This, of course, varies under different climactic conditions, and the changes produced are the same as those imposed by heat from any source. Circulatory changes are known to result from the heat absorbed. Systemic circulatory changes may also result from sunburn itself, with a lowering of the blood pressure and a slight increase in cardiac output, probably from general peripheral arteriolar dilatation. This may be due to the release of leukotaxine or some similar substance, which causes a generalized lowering of capillary permeability. Ultraviolet radiation

with wave length through the near ultraviolet region and is high throughout the visible spectrum, considerable amounts of visible radiation reaching the corneum and even the subcutaneous tissue. Transmission remains high in the near infrared region, but deep indentations appear in the transmission curve at wave lengths corresponding to maximum absorption by water. At the wavelength limit of sunlight, 3000 millimicrons, penetration is extremely slight. There is considerable disagreement concerning the maximum values for penetration from 700 to 1500 millimicrons. The temperature of the tissues at some depth may be raised appreciably when radiation impinges on the

mined by the kind of molecules present in the environment, as well as by the activated molecule. The effect may be characterized by an action spectrum, meaning that light of certain wave lengths is specifically absorbed and leads to the activation of molecules. Action spectra may follow absorption spectra so closely that absorbing compounds can thus be identified.

Exposure of the skin to bright summer sunlight for a half-hour or longer is followed by dilatation of vessels and objective erythema and slight swelling. Following prolonged exposure the edema may be marked, with desquamation and blistering and pain or itching. The erythema fades in a few days

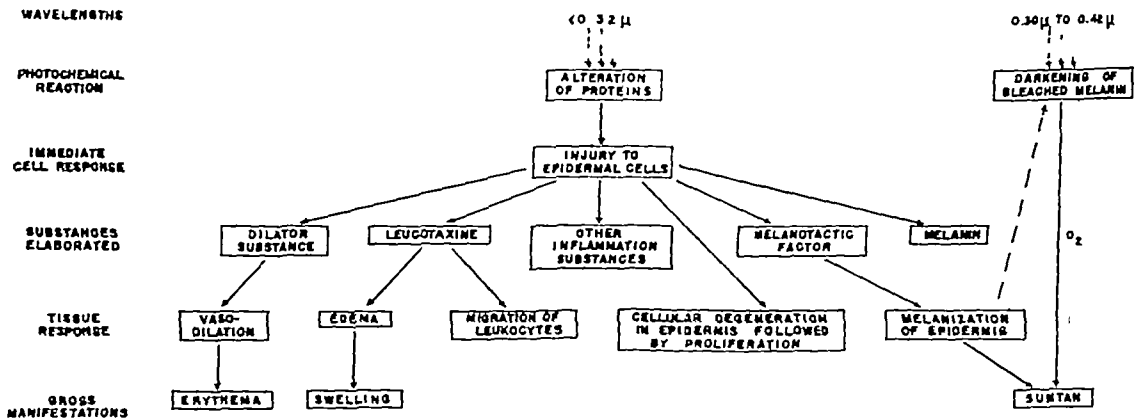


FIGURE 1 Mechanism of Sunburn (Blum<sup>29</sup>)

skin surface, but this does not indicate actual penetration of the incident radiation. Some of the high values may actually be due to conductive heating. Even if the highest values obtained could be accepted, it is not conceivable that an important fraction of sunlight reaches skin tissues more than a few millimeters beneath the surface. Light of wave lengths that produce the most striking effect in human skin in sunburn penetrates only a small fraction of a millimeter. A large proportion of total sunlight is reflected by human skin, the percentage varying with different complexions. There is no reflection of wave lengths longer than those found in sunlight, the total radiation being absorbed extremely superficially. The human body itself emits a broad band of wave lengths, with a maximum at about 10 microns. In this spectral region human skin behaves as a perfect radiator or black body.

### Physiologic Effects

The specific effects of sunlight, particularly ultraviolet radiation, are initiated by a photochemical reaction, as contrasted with the radiant heat effects that result from a local rise in temperature. The photochemical reaction is dependent on activation of molecules by the capture of quanta of radiation. The type of chemical reaction that follows is deter-

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and is replaced by pigmentation, with an increase of melanin in the epidermis. Blum<sup>29</sup> has postulated that sunburn is due to direct injury to the cells of the epidermis by ultraviolet radiation, and that as a result of injury the cells elaborate various substances that bring about specific physiologic responses. These substances are elaborated at slow rates, thus accounting for the long latent period between exposure and the appearance of erythema. A scheme illustrating the sequence of events in sunburn is shown in Figure 1.

Ultraviolet radiation is known to produce injurious effects in living systems in general. Special studies have been made of the effects of ultraviolet radiation on single cells, such as bacteria, protozoa, sperm and eggs. Action spectra indicate that ultraviolet radiation exerts an injurious action by altering either protein or nucleic acid. The erythema of sunburn is generally credited to the action of a histaminelike dilator substance released by the injured cells, the exact chemical nature of which is unknown. The increased capillary permeability may be due to a substance called by Menkin,<sup>30</sup> "leucotaxine," which brings forth migration of leukocytes and tissue edema. Other changes in sunburned skin include an increase in surface temperature, changes in electrical potentials, an increase

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The President read the following obituaries:

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Dr Timmins is survived by his widow, two sons and two daughters.

**McNAMARA.** Dr John J McNamara died on January 3, 1946. He was seventy-five years old at the time of his death. He was a New Yorker by birth but was adopted by Massachusetts more than sixty years ago. He received his medical education at Tufts College Medical School, obtaining his medical degree in 1900. From his early days he was a man of singular industry and alertness, an athlete-scholar who played both baseball and football for his college as a medical student and at the same time served as an assistant in the Department of Chemistry.

He entered practice in Brockton. As a practitioner his interest in sportsmanship continued for many years, and his appearance at the Brockton Fair, driving in a sulky behind a trotting horse, came to be looked on as one of the Fair's important annual features. He was always a genuine patriot, in 1912 he was appointed by Governor Foss as associate medical examiner, during World War I he served as captain in the Medical Corps of the Army, and more recently he had been physician for the Veterans Bureau.

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mittee meeting said that this arrangement was working well. He added that a committee of physicians from the district society sat in judgment on disputed bills and that its decisions were accepted by all concerned.

The representative for the Norfolk South District Medical Society said that a similar arrangement was in operation in his community and that it even applied to welfare cases that were being treated in hospitals having regular staffs.

The Executive Committee recommends the adoption of this recommendation and such others as are contained in this report.

The Executive Committee reviewed the report of the Committee on Legislation and recommends its acceptance.

The Executive Committee has reviewed the report of the Committee on Cancer. It approved the report and the recommendation contained in it.

The Executive Committee has reviewed the report of the Committee on Medical Defense. As it interprets this report, it contains a recommendation that a committee be set up for the purpose of reviewing the subject of malpractice insurance. The Executive Committee approved this report and the recommendation contained in it.

The Executive Committee reviewed the report of the Committee on Ethics and Discipline and that of the Medical Advisory Committee to the Regional OPA. It approves of both.

The Executive Committee has reviewed the report of the Committee on Public Health. It noted that the chairman of the committee wished to amend the recommendation contained in it so that the Council is now asked to approve the committee's sending a letter, through and at the expense of the American Epilepsy League, Incorporated, to all the physicians in Massachusetts, offering literature on the latest advances in the treatment of epilepsy to those who are interested.

The Executive Committee approves of this change because it believes the original language would involve the Society in a commitment which it should not be asked to assume.

Action on this recommendation will be sought when the report of the Committee on Public Health is formally before the Council.

The Executive Committee reviewed the report of the Committee on Postwar Planning. It approved the report and the recommendations contained in it. It recommends that two additional recommendations be added to this report, namely:

That the Council authorize the President to appoint a special committee for the purpose of initiating plans for a postgraduate assembly in 1946.

That the Council, with the approval of the Committee on Finance, authorize an extraordinary appropriation of one thousand dollars for the use of this committee.

Action on these additional recommendations will be sought when the report of the Committee on Postwar Planning is formally before the Council.

The Executive Committee has reviewed the report of the Military Postgraduate Committee. It approves of this report and, in recommending the adoption of the committee's recommendation that it be discharged, would add the words, "with thanks."

The Executive Committee reviewed the report of the Committee on Council Rules. It approves of the recommendations contained in it.

The Executive Committee reports that a motion recommending that the Council set the membership dues at \$20.00 per year beginning in 1947 was laid on the table until the next meeting of the committee.

The Secretary moved the adoption of the report as a whole. This motion was seconded by Dr. Carl Bearse, Norfolk, and it was so ordered by vote of the Council.

*Committee on Finance* — Dr. Francis C. Hall, Suffolk, chairman.

This report (Appendix No. 2) was submitted by the chairman. He moved the adoption of the report

and the budget submitted. This motion was seconded by Dr. Peirce H. Leavitt, Plymouth.

The President, in commenting on the budget, said that it represented the largest ever submitted.

Dr. Hall's motion was adopted by vote of the Council.

*Committee on Public Relations* — Dr. Albert A. Hornor, Suffolk, secretary.

This report (Appendix No. 3) was submitted by the secretary of the committee who moved its acceptance. This motion was seconded by Dr. Roy J. Heffernan, Norfolk.

Dr. Cheever asked whether or not the term "community hospitals" as used in the report meant tax-supported hospitals. Dr. Hornor replied that they referred to any hospital serving a community whether tax-supported or otherwise.

The motion to accept the report was adopted by vote of the Council.

The President said that the report contained many recommendations. The first requested that the Council adopt a plan whereby certain licensed physicians in Massachusetts, who have graduated from unapproved medical schools, may obtain hospital privileges in certain community hospitals. He added that the plan, to be effective, entails approval by the American College of Surgeons, the American Medical Association and the Massachusetts Hospital Association, as well as that of the Council of the Massachusetts Medical Society.

Dr. Hornor moved that the Council adopt the plan as outlined in the report. This motion was seconded by Dr. H. Quimby Gallupe, Middlesex South. Dr. Gallupe made a strong and effective plea for the adoption of this plan.

Dr. Allen G. Rice, Hampden, asked for a definition of the terms "staff meetings" as they appear in the report. Dr. Hornor said that these terms referred to meetings of the staff as a whole wherein were studied interesting and difficult cases, where deaths were analyzed and the whole professional conduct of the hospital reviewed.

Dr. Rice asked whether or not these terms meant that those covered under this plan would be invited to attend staff meetings where officers were elected and new appointments and promotions were considered. Dr. Gallupe, in replying to this question, said that the functions outlined in Dr. Rice's question represented the duties of an executive committee of the staff rather than that of the staff as a whole and that the terminology used in this report referred to the educational meetings of the staff wherein only the professional activities of the hospital were reviewed.

The plan as outlined was adopted by vote of the Council.

The Secretary moved the adoption of the recommendation of the Executive Committee to the effect that the activation of this plan be through the Committee Appointed to Confer with the Massachusetts

water-pitcher, which he hoped thereafter would always be used at Cotting luncheons. The pitcher had been given him in token of friendship by Dr. George Hayward, secretary of the Society from 1826 to 1832 and president from 1852 to 1855. The growth in size of the Council and the change in character of the luncheons have made it difficult to carry forward Dr. Cotting's wishes in regard to the pitcher. It is in attendance at today's meeting, however, out of deference to his desires.

The Secretary presented the record of the last stated meeting of the Council held on October 3, 1945, as published in the *New England Journal of Medicine*, issue of December 20, 1945. He moved its acceptance. This motion was seconded by Dr. David Cheever, Suffolk, and it was so ordered by vote of the Council.

## REPORTS OF COMMITTEES

*Executive Committee* — Dr. Michael A. Tighe, Middlesex North, secretary

This report, which was submitted by the Secretary, is as follows:

The report of the Executive Committee of the Council has already been sent to each councilor. This has been done in anticipation of the adoption of a new rule which will make such action mandatory on the part of the Secretary. Under this rule not only will the action of the Executive Committee be reported in advance but likewise there will be presented in advance a résumé of the discussion attending any important subject before the committee.

It is hoped that this may be a means of anticipating and answering many questions, the asking and answering of which consume much of the Council's time.

The Secretary regrets that, owing to circumstances over which he had no control, when the original report of the Executive Committee of the Council was sent out, the résumé of the discussion which attended two important subjects could not be included. These résumés will appear in their proper setting in the report which will now be submitted.

The Executive Committee of the Council reviewed the reports of the Committee on Finance and the budget submitted by the committee for the year 1946. It approves of the budget and of the recommendations contained in this report.

The Executive Committee has reviewed the report of the Committee on Public Relations.

The first recommendation contained in this report has to do with a plan whereby graduates of approved schools who are licensed to practice medicine in Massachusetts may be permitted to care for their patients in approved hospitals and participate in certain other activities of such hospitals. This plan in no way attempts to dictate to any hospital what its policy shall be. It recognizes that, already, certain hospitals have adopted this plan or some modification of it and that others might be encouraged to do likewise. This plan realizes the teaching possibilities which are inherent in all hospitals and the necessity of utilizing these possibilities in the interest of good medical care for all the people of the community.

In the discussion, which attended the subject, it was said that two out of every seven licensed physicians in Massachusetts were graduates of unapproved medical schools, that the medical care of many thousands of Massachusetts citizens was in the hands of such graduates and that many of them are in need of the additional training which may be had by some form of association with a good hospital.

It was further brought out that, at least for the moment, the unapproved schools in Massachusetts have been discontinued. While no one could say what the future holds in this respect, it was the tendency of the committee to regard it as a problem which was closed, leaving finally to be dealt with a backlog of imperfectly trained physicians who needed our help if the people of the Commonwealth were to have the kind of medical care to which they were entitled.

What would be the attitude of the Council on Hospitals and Medical Education of the American Medical Association if the hospitals of this state were to adopt some such plan? Would such hospitals lose their rating as hospitals approved for intern training? These are some of the questions to which the committee directed its discussion.

While it was indicated that, until some such formal plan as outlined was approved by the Massachusetts Medical Society and presented to the Council on Hospitals and Medical Education, no formal action might be expected from this source, it did come out that the plan had been informally discussed with the secretary of the Council on Hospitals and Medical Education of the American Medical Association and that he thought it represented a practical way of cleaning up a bad situation. He also expressed it as his opinion that the Council on Hospitals and Medical Education would not penalize the hospital that adopted it.

The attitude of the American College of Surgeons has not been ascertained but here, too, it is unlikely that the plan would be formally approved, pending its approval by the Massachusetts Medical Society.

It was the opinion of the committee that, while not all would avail themselves of the privileges called for in the plan, many might be expected to do so.

Finally, it was also the opinion of the committee that it was much more desirable for the hospitals to voluntarily adopt some such plan as this rather than run the risk of having their doors forced open by legislative enactment.

The Executive Committee recommends that the Council approve this plan.

In the event that this plan is approved when it is formally before the Council, the Executive Committee recommends that its activation shall be through the Committee Appointed to Confer with the Massachusetts Hospital Association.

The second recommendation contained in this report deals with certain principles which should govern the relation of the United States Veterans Administration, civilian physicians and civilian hospitals in the medical and hospital care of those for whom this administration is responsible.

The Executive Committee took note of the tremendous problem which confronts the Veterans Administration in this regard and the Administration's utter inability to meet the requirements of the law without the active and wholehearted co-operation of the civilian physician and civilian hospital. The Committee on Public Relations, in noting the emergency character of the problem involved, made representations to the President dealing with the necessity of immediate action. In compliance with such representations, the Executive Committee noted that the President appointed a committee of the Society to confer with Major General Paul R. Hawley, Acting Surgeon General of the Veterans Administration.

The Executive Committee approved of this act of the President. It recommended that the Council do likewise.

The Secretary moved the adoption of this recommendation. This motion was seconded by Dr. Albert A. Hornor, Suffolk, and it was so ordered by vote of the Council.

The Secretary continued the report as follows:

The last recommendation contained in the report of the Committee on Public Relations is to the effect that, if at any time the Massachusetts Medical Society recommended that the prevailing rate of fees be reduced for the medical care of tax-supported cases, this action be rescinded.

The discussion attending this subject indicated that in May, 1945, the Executive Committee, acting for the Council, approved of the policy of paying physicians for the care of welfare cases in unstaffed hospitals at the rate of \$4.00 for the first visit and \$2.00 for each succeeding visit, not to exceed a total sum of \$150.00. It came out in the discussion that the Franklin District Medical Society had long since arranged for the payment of regular fees in tax-supported cases. The representative of the Franklin District Medical Society present at the com-

Dr Moore moved the adoption of the report as a whole. This motion was seconded by Dr Hall, and it was so ordered by vote of the Council.

*Committee on Medical Defense* — Dr Arthur W Allen, Suffolk, chairman

In the absence of Dr Allen, the Secretary submitted the report (Appendix No 6) as published and moved its acceptance. This motion was seconded by Dr Bagnall, and it was so ordered by vote of the Council.

The President said that this report contained two recommendations as follows:

That a special committee of five be appointed by the President to review the matter of malpractice insurance; the report of such a committee to be submitted at the next meeting of the Council.

That the Secretary shall notify Mr Nolan that the proposal to the Society outlined in his letter of November 17, 1945, is under advisement.

The Secretary moved the adoption of these recommendations. This motion was seconded by Dr Bagnall, who spoke of a conversation which he had a year ago with the President of the Pennsylvania State Medical Society about the cost of malpractice insurance in that state. He said that the latter said they had a very happy situation in that state, where the coverage costs as little as \$8.00 per year.

Dr Hornor moved as an amendment to the motion to adopt that the committee appointed under these recommendations be given authority to employ counsel if, in its opinion, such employment is deemed necessary. This amendment was seconded by a councilor.

Dr Bearse said that a previous attorney general of Massachusetts had ruled that group insurance along this line is illegal in Massachusetts.

The motion as amended was adopted by vote of the Council.

The Secretary moved the adoption of the report as a whole as amended. This motion was seconded by Dr John B Hall, and it was so ordered by vote of the Council.

*Committee on Ethics and Discipline* — Dr Ralph R Stratton, Middlesex East, chairman

This report, which is as follows, was offered by the chairman:

The work of the Committee on Ethics and Discipline since the last meeting has been merely one of routine and requires no report at this time.

The following letter was referred by the Council to the Committee on Ethics and Discipline:

October 1, 1945

Reginald Fitz, M.D.  
319 Longwood Avenue  
Boston, Massachusetts

Dear Dr Fitz:

We wish to employ at the Newton Hospital a doctor who has only a dental degree. For a number of years he was engaged in the practice of oral surgery in Boston, returning before the war. Since Pearl Harbor he has put in a little over a year as a volunteer anesthetist and has carried out that work very efficiently and has met the approval of the surgeons with whom he has worked.

Our question is: Is it proper for a man possessing a dental degree to work as an anesthetist in the Newton Hospital under my supervision?

We would appreciate an early answer. Thanking you I am

Sincerely yours

R. S. Hunt, M.D.  
Anesthetist in Chief

It was moved by Dr Rice and seconded by Dr Gardner that, because of the shortness of trained anesthetists and because of the present emergency, it is not unethical to employ the dentist mentioned in the communication provided his work is supervised by Dr Hunt. It was so ordered by vote of the committee.

Dr Stratton moved the acceptance of the report. This motion was seconded by Dr Charles E. Mongan, Middlesex South, and it was so ordered by vote of the Council.

Dr Stratton said the Committee on Ethics and Discipline received a letter, addressed to the President, from Dr R. S. Hunt, of the Newton Hospital. This letter, he added, was reproduced in the committee's report, as was the action of the committee with regard to it. He moved that the Council approve of this action of the committee. This motion was seconded by Dr Bearse, and it was so ordered by vote of the committee.

Dr Stratton moved the adoption of the report as a whole. This motion was seconded by Dr Leavitt, and it was so ordered by vote of the Council.

*Medical Advisory Committee to Regional OPA* — Dr Joseph Garland, Suffolk, chairman

This report, which is as follows, was offered by the chairman:

This committee held its latest and perhaps its last full meeting on September 20, 1945. At that time, so soon after the war's ending, processed food had already gone off rationing and rationing had been relaxed on red-point foods. Applications, however, continued to come in, particularly for extra sugar.

On November 23 the day after Thanksgiving, rationing was finally abandoned on all foods except sugar. Sugar will remain scarce until the Philippine crop is available, and will probably continue to be rationed, according to our advices, until April, 1946. Until then, this committee will need to function to some degree. The present allotment of sugar is one-fourth pound weekly per individual.

It apparently seems unfortunate to certain people that privations must continue to exist in the postwar world but we believe that they can be guaranteed against any unusual health hazard even if their requests for extra sugar are ordinarily denied.

This report is offered for the information of the Council.

Dr Garland moved the acceptance of this report. This motion was seconded by Dr John B Hall, and it was so ordered by vote of the Council.

Dr Stratton moved the adoption of the report. This motion was seconded by Dr Felton, and it was so ordered by vote of the Council.

*Committee on Public Health* — Dr Roy J Ward, Worcester, chairman

This report (Appendix No 7) was offered by the chairman, who moved its acceptance subject to the recommendation of the Executive Committee. This motion was seconded by Dr Bagnall, and it was so ordered by vote of the Council.

Dr Ward moved the adoption of the report subject to the amendment recommended by the Executive Committee. This motion was seconded by Dr Bagnall. This recommendation is to the effect that the Council approve the Committee on Public Health sending a letter, through and at the expense of the American Epileptic League, Incorporated, to

Hospital Association Dr Hornor seconded this motion, and it was so ordered by vote of the Council

The President said that the second recommendation contained in the report of the Committee on Public Relations was to the effect that the Council affirm its belief, in answer to the Honorable Philip J. Philbin, that the most satisfactory and economical care of veterans in Massachusetts can be obtained by granting them right to free choice of licensed physicians, at prevailing rates in their own communities, and, if hospitalization is required, in local licensed hospitals of their own choice, and that each district society be advised to appoint a special committee authorized to meet on call by the Veterans' Bureau to adjust any disputes or difficulties that might arise under such a program

Dr Hornor moved the adoption of this recommendation This motion was seconded by Dr Charles J. Kickham, Norfolk, and it was so ordered by vote of the Council

The President outlined the third recommendation contained in this report as follows

That each district society shall be advised to appoint a special committee to act in an advisory capacity with local boards of public welfare so that recipients of Old Age Assistance may have free choice of physicians and so that physicians so employed may be properly paid for their services

Dr Hornor moved the adoption of this recommendation

In seconding this motion Dr John J. Dumphy, Worcester, said that there is a new provision in the law which requires that welfare recipients be allowed free choice of physician He said that the Commissioner of Public Welfare in Boston took the initiative in this matter and sought a meeting with the Subcommittee on Tax-Supported Medical Care and that this committee had turned the problem, as it related to Boston, over to the Suffolk District Medical Society

He added that the commissioners of public welfare in other communities might not take this same initiative and that he believed other districts should be urged through the instrumentality of the provision of this recommendation to seek out their respective commissioners, so that this provision of the law might be fully realized

The motion was adopted by vote of the Council

The President outlined the fourth and final recommendation of the Committee on Public Relations as follows

That if, at any time, the Council of the Massachusetts Medical Society recommended that the prevailing rate of fees be reduced for the medical care of tax-supported care, this action be rescinded

Dr Hornor moved the adoption of the recommendation This motion was seconded by a councilor

Dr Dumphy urged the rejection of the recommendation He said that it had never been con-

sidered by the Subcommittee on Tax-Supported Medical Care that its adoption would put the whole profession in an undesirable light before the public

Dr Elmer S. Bagnall, Essex North, said he supported this recommendation in principle but not in practice He thought its adoption at this time might precipitate great difficulties He thought the matter involved would be better handled on a local level and that while the recommendation did not make it mandatory that local groups insist on full fees for the care of the cases involved, he thought it unwise to adopt the recommendation at this time

Dr Leroy E. Parkins, Suffolk, amended the motion to adopt so as to provide for the deletion of the word "rescinded" as it appears at the end of the recommendation and the substitution of the words "reviewed by the Subcommittee on Tax-Supported Medical Care" This amendment was seconded by Dr Bagnall

Dr Hornor said that this matter had been discussed fully in the Committee on Public Relations and that it came out that certain districts were acting on the basis of full fees for tax-supported medical care, that this seemed to be in conflict with a former vote of the Council of the Massachusetts Medical Society and that the recommendation was brought in for the purpose of removing the conflict

The motion as amended was adopted by vote of the Council

Dr Hornor moved the adoption of the report as a whole, as amended This motion was seconded by Dr Cheever, and it was so ordered by vote of the Council

*Committee on Legislation* — Dr Reginald Fitz, Suffolk, acting chairman

The President said that this report (Appendix No 4) was informational only

Dr Bearse moved its adoption This motion was seconded by Dr James P. O'Hare, Suffolk It was so ordered by vote of the committee

*Committee on Cancer* — Dr George A. Moore, Plymouth, chairman

This report (Appendix No 5) was presented by the chairman, who moved the acceptance of the report as printed This motion was seconded by Dr John B. Hall, Norfolk It was so ordered by vote of the Council

The President said the report contained one recommendation, which was to the effect that the Council endorse, in principle, instruction about the disease cancer in the public schools of Massachusetts

Dr Moore moved the adoption of the recommendation This motion was seconded by a councilor

Dr Lester M. Felton, Worcester, in registering his opposition to this recommendation, questioned its value The recommendation was adopted by vote of the Council

The first matter considered by the committee had to do with the question of establishing a rule of the Council which would require district councilors to meet and discuss the agenda prior to regular Council meetings. It was voted by the committee not to establish this as a rule but to recommend that the district councilors follow this procedure.

The second matter that was discussed had to do with the report of the Executive Committee. It was believed that this report should contain a resumé of the discussion which took place before the Executive Committee in matters of particular importance. The committee voted to recommend to the Council that a rule providing for such be set up. The committee also voted to recommend to the Council that a further rule be created which would require the Secretary to send to the councilors a week before the Council meeting the report of the Executive Committee.

The Secretary said that these new rules would require the services of a stenographer at the meetings of the Executive Committee. He recommended that the Committee on Council Rules ask the Committee on Finance for an additional appropriation for the Secretary's office of \$150 to cover such costs.

Dr Mongan moved the acceptance of the report. This motion was seconded by Dr Bearse, and it was so ordered by vote of the Council.

The President said that this report, as interpreted by the Executive Committee, contained several recommendations. He stated the first as follows:

That the Secretary shall be directed by the Council to write annually to each district society president, shortly after the latter's election to office, suggesting that the councilors from his district society be asked to meet regularly, prior to Council meetings, to discuss the agenda of each meeting.

Dr Mongan moved the adoption of this recommendation. This motion was seconded by Dr Bagnall, and it was so ordered by vote of the Council.

The second recommendation contained in this report is that two additional rules for its government be adopted by the Council. The first is to be known as Rule 7. This provides that the secretary of the Executive Committee shall prepare a report of each regular meeting of the committee which shall contain an abstract of the discussions and actions of the committee on all matters of particular importance. The second, to be known as Rule 8, provides that the abstract mentioned in Rule 7 be sent to each councilor at least a week before each meeting of the Council.

Dr Mongan moved the adoption of these recommendations. This motion was seconded by Dr Smith, and it was so ordered by vote of the Council.

Dr Fitz said that, with regard to the final recommendation, which called for funds to cover the additional costs made necessary by the adoption of Rules 7 and 8, the Committee on Finance had already acted.

Dr Mongan moved the adoption of the report as a whole. This motion was seconded by Dr Leavitt, and it was so ordered by vote of the committee.

A motion to adopt a report of no report from the following committees was made by Dr Smith and seconded by Dr Felton: Arrangements, Industrial

Health, Medical Education, Nominations, Publications, Society Headquarters, Expert Testimony, To Confer with the Massachusetts Farm Bureau Federation, Maternal Welfare, To Meet with the Massachusetts Hospital Association, To Nominate a Director of Medical Information and Education, To Recommend Blue Shield Directors, Physical Medicine, Postwar Loan Fund and Rehabilitation. The motion was carried by vote of the Council.

The President reminded the Council that, at the stated meeting on October 4, 1944, the Committee on Expert Testimony rendered a report which moved that a standing committee of five or more be appointed by the President, to be called the Committee on Medicolegal Problems and that the by-laws be amended to provide for such a body. The report was received, the President continued, and its motion was warmly debated. The motion was disposed of by being laid on the table. The committee has not reported since that date. The President suggested that action was in order to take this motion from the table so that the Committee on Expert Testimony might feel no restraint in resuming its activities in any manner it deemed proper.

Dr Leavitt moved to take the matter referred to by the President from the table. This motion was seconded by Dr Smith, and it was so ordered by vote of the Council.

#### APPOINTMENTS BY THE PRESIDENT

Under the provisions of Chapter IV, Section 7, of the by-laws of the Massachusetts Medical Society, and Chapter I, Section 2, of the by-laws of the American Medical Association, the President nominated the following as delegates and alternates to the House of Delegates of the American Medical Association to serve from June 1, 1946 to June 1, 1948:

DELEGATES	ALTERNATES
Charles E. Mongan, Middlesex South	Patrick E. Gear, Hampden
Dwight O'Hara, Middlesex South	William J. Pelleter, Franklin
Walter G. Phippen, Essex South	John I. B. Vail, Barnstable
David D. Scannell, Norfolk	Elmer S. Bagnall, Essex North

There being no nominations from the floor, the Secretary was instructed to cast one ballot confirming the nomination of those named by the President. The Secretary announced that he had complied with this directive, and the President declared the above elected.

The President announced that, under Chapter IV, Section 7, of the by-laws of the Massachusetts Medical Society, he nominated the following councilors to serve as delegates to the annual meetings in 1946 of the other New England state medical societies:

Connecticut: Frederick S. Hopkins, Hampden, Clement F. Kernan, Berkshire.  
Maine: Frank R. Ober, Suffolk, Merrill C. Sosman, Suffolk.  
New Hampshire: Dwight O'Hara, Middlesex South, Howard F. Root, Suffolk.

all physicians in Massachusetts offering literature on the latest advances in the treatment of epilepsy to those who are interested

The motion was carried by vote of the Council  
*Committee on Postwar Planning* — Dr Howard F Root, Suffolk, chairman

The Secretary offered this report (Appendix No 8) in the absence of Dr Root and moved its acceptance This motion was seconded by Dr Felton, and it was so ordered by vote of the Council

The President said that the report contained three recommendations

The first he outlined as follows

That the Council, in accordance with its previous action, shall inform the Committee on Education and Labor of the United States Senate and other appropriate authorities of its belief that the Federal Government should establish a Department of Health and Welfare with a secretary in the President's Cabinet, under whom will be co-ordinated all important health and welfare programs, exclusive of those of the Army and Navy, the Division of Health being under the direction of a physician

Dr Richard M Smith, Suffolk, moved that the recommendation be tabled This motion was seconded by a councilor, and it was so ordered by vote of the Council

The above action was taken because, during the debate attending this subject, it seemed to many that there were other governmental departments which should be excluded from the provisions of the recommendation and because the Council did not deem itself sufficiently informed at the moment to name such departments

The President outlined the second recommendation as follows

That the Society shall offer its services, through a special committee of five appointed by the President, to the Council on Medical Education and Hospitals of the American Medical Association to assist that council in the provisional approval for internships and residencies of certain Massachusetts hospitals

Dr Felton asked the meaning of the term "certain Massachusetts hospitals" The President replied that it referred to those hospitals that might seek such approval

The Secretary moved the adoption of this recommendation The motion was seconded by a councilor, and it was so ordered by vote of the Council

The President outlined the third recommendation, as amended by the Executive Committee, as follows

That the Council initiate plans for a postgraduate assembly in 1946 through a special committee of five appointed by the President and that an extraordinary appropriation of \$1000 be made for this purpose with the approval of the Committee on Finance

The Secretary moved the adoption of this recommendation This motion was seconded by a councilor

Dr Parkins moved as an amendment "that other state societies of New England be invited to participate as before the war" This amendment was seconded by a councilor

The recommendation as amended was adopted by vote of the Council

Dr W Richard Ohler, Norfolk, moved the adoption of the report as a whole as amended This motion was seconded by Dr Frank R Ober, Suffolk, and it was so ordered by vote of the Council

*Military Postgraduate Committee* — Dr W Richard Ohler, Norfolk, chairman

The report, which is as follows, was submitted by the chairman

Postgraduate instruction for men in the armed services throughout the country ceased with the close of 1945 In so far as the work of your committee is concerned, the last programs were given in November, 1945

Postgraduate military instruction started in Massachusetts in November, 1942, and was directed by the Military Postgraduate Committee of the Massachusetts Medical Society In the spring of 1943 the American Medical Association, the American College of Physicians and the American College of Surgeons inaugurated a program of postgraduate medical instruction for physicians in the armed services throughout the country By mutual consent and as a result of very pleasant co-operation on the part of all concerned, it was agreed during the summer of 1943 to centralize all the work of providing military postgraduate instruction throughout New England into one committee to be known as the New England Committee for Wartime Graduate Medical Meetings The work of this committee was sponsored by the medical societies of all the New England states together with the American Medical Association, the American College of Physicians and the American College of Surgeons It is to the credit of the Massachusetts Medical Society that this work was started a full year prior to the organization of the national body

Since the fall of 1942, four hundred and twenty-eight postgraduate sessions have been given in twenty three Army, Navy and Coast Guard installations throughout New England There is plenty of evidence indicating that this work has been tremendously appreciated by the armed services It goes without saying that the success of the program in New England results from the unselfish efforts of the many instructors who took part in these programs

It is recommended that the committee be discharged

It is further recommended that a copy of this report be sent to the other New England state medical societies

Dr Ohler moved the acceptance of the report This motion was seconded by Dr Ober, and it was so ordered by vote of the Council

The President pointed out that the report, as amended by the Executive Committee, contained two recommendations

That the committee be discharged with the thanks of the Society

That copies of the report be sent to the military postgraduate committees of the other state medical societies of New England

Dr Smith moved the adoption of the recommendations as amended This motion was seconded by Dr Felton, and it was so ordered by vote of the Council

Dr Ober moved the adoption of the report as a whole as amended This motion was seconded by Dr Ohler, and it was so ordered by vote of the Council

*Committee on Council Rules* — Dr Charles E Monagan, Middlesex South, chairman

The report, which is as follows, was offered by the chairman

which Dr Baty intended to offer might be all right but that he for one could not conscientiously vote on it without more information than had been submitted

Dr Baty said that, although the survey was going to be made whether the Council approved of it or not, it would help greatly if it had the approval of the established medical organization in Massachusetts

Dr Smith said that the pediatricians felt that there had been a good deal of intrusion by governments in pediatric practice and that justification for this intrusion was based on certain statements which might be true or might not be true. He added that it was the purpose of the Academy, in making this survey, to ascertain the true facts. He thought it desirable that the Council should give its blessing to such an undertaking

Dr Bagnall urged the suspension of the rules because it should not be said of the Council that it would not co-operate in fact finding

Dr William E. Browne, Suffolk, asked Dr Baty if he knew of this matter of the survey before the last Executive Committee meeting. Dr Baty replied that he did not. He added that it was within three days that he had been appointed Massachusetts chairman

Dr Browne asked Dr Baty if he believed that this fact finding could be completed quickly enough to be a factor affecting the deliberations of the senate with regard to Senate Bill 1318

Dr Baty said that such a survey had been completed in North Carolina in six weeks and that, although the actual analysis of the data accumulated could undoubtedly take a longer time, there would be certain factual determinations which could be used much earlier

Dr McCarthy registered his opposition to suspending the rules

By a standing vote the Council voted to suspend the rules and give immediate consideration to the subject of Dr Baty's communication

Dr Baty moved that the Council of the Massachusetts Medical Society approve of the survey of the Children's Health Services which is being undertaken by the American Academy of Pediatrics. This motion was seconded by Dr Felton

Dr Norman A. Welch, Norfolk, asked for a brief explanation of just what the survey consists of and how extensive it is intended to be

Dr Baty replied as follows

The way the survey worked in North Carolina, and the way we hope that it will work here, is that a full-time paid executive was appointed to cover the study. He and the state chairman of the Academy of Pediatricians worked in conjunction, first, with the pediatricians in the state who are members of the Academy. They attempted to obtain information concerning pediatric practice, the number of children seen by physicians and so forth

The thing we are trying to find out first is how much hospitals are doing. We are attempting to collaborate our hospital survey with the one that is being carried on

nationally at the moment, and for that reason in some states we are already beginning to collect data by utilizing the findings of the regular hospital survey

We then want to find out how much in the way of care of children both pediatricians and family physicians or general practitioners are doing, as well as the number of children being seen in clinics, and what type of service is being rendered

We hope to be able to determine in some way the quality of medical care that is being rendered in hospitals, that will be difficult so far as individuals are concerned, but in hospitals we hope that the pediatricians on the staffs, by filling out the forms, will assist us materially. We are drawing up elaborate questionnaires, regarding participation of various individuals, staff meetings and various things that Dr Gallupe mentioned in offering assistance to the graduates of substandard schools. In that way we hope to find out the answers to many of these questions

The way they collected the data about practice in North Carolina was to ask the pediatricians to supply, for a certain period, data concerning the children that they saw in hospitals, in homes and in their offices. We hope to obtain that information from pediatricians, as well as from certain other physicians

We recognize that only a small proportion of medical care to children is rendered by members of the Academy, indeed, the great majority is given by general practitioners

Dr Baty said the Academy was opposed to both Senate Bill 1318 and Senate Bill 1606 and that its suggestions regarding legislation were based almost entirely on the recommendations of the Massachusetts Medical Society

Dr McCarthy asked how this survey was to be financed. Dr Baty replied that he could not answer this exactly but that the total budget would undoubtedly run somewhere around a million dollars. The Academy, he continued, could furnish only a relatively small amount of that sum. Dr John Hubbard was being paid by the Academy a full-time salary, and not a small salary, for his part of the work. The Academy had raised that money out of its own funds, and would raise certain of the other moneys. He added

Some of the funds that are going toward this have been and are being donated by private philanthropic organizations. A great deal of the money will have to be raised locally, and it will be raised in various ways

A good many of the things that we are trying to find out other organizations want to know. At the moment the Council of the Greater Boston Community Fund is very anxious to find out about health services for children among the organizations that they support, and they have appointed a committee and have allotted a budget to carry out this work

The survey was successful in North Carolina, and we believe that it will work here. We are having conferences with various organizations, and we believe that these organizations will help in carrying out certain of the work, that is, that they will supply money. We hope that other types of organizations, such as those assisting crippled children, may, in many states, supply some of this money.

The motion was adopted by vote of the Council

Dr Parkins moved the suspension of the rules so as to permit an informational report concerning the Bureau of Clinical Information (Appendix No 10) to be made part of the record of the meeting. This motion was seconded by Dr Baty, and it was so ordered by vote of the Council

Dr C. J. E. Kickham, Norfolk, asked when the resolution submitted by the Norfolk District Medical

*Rhode Island* W Richard Ohler, Norfolk, Leroy E Parkins, Suffolk  
*Perrmont* George Ballantyne, Worcester, William A R Chapin, Hampden

There being no nominations from the floor, the Secretary was instructed to cast one ballot approving the nominations as made by the President. The Secretary announced that he had complied with the directive and the President declared the above elected.

The President nominated Dr H Quimby Galupe, Middlesex South, as delegate for 1946 to the Annual Congress on Medical Education and Licensure of the American Medical Association. This nomination was confirmed by vote of the Council.

The President made the following *ad interim* nominations:

A Price Heusner, Boston, councilor for the Suffolk District, to succeed Edward F Timmins, deceased  
 Alfred L Duncombe, Brockton, councilor for the Plymouth District, to succeed John J McNamara, deceased  
 Lewis M Hurxthal, Boston, censor for the Suffolk District, to succeed Edward F Timmins, deceased  
 Peirce H Leavitt, Brockton, member of the Committee on Legislation representing Plymouth District, to succeed John J McNamara, deceased

The President named Dr Bancroft C Wheeler, Worcester, to the Committee on Finance to succeed Dr Ernest L Hunt, resigned. The President, in making this latter nomination, said that he had accepted Dr Hunt's resignation with very real regret. He described him as a loyal and devoted servant, never self-seeking and always working for the Society's good.

Dr Bagnall moved confirmation of these appointments. This motion was seconded by Dr Hornor, and it was so ordered by vote of the Council.

The President announced the resignation of Mr Manfred Bowditch from the Advisory Committee to the Committee on Industrial Health, this resignation being made necessary by reason of Mr Bowditch's departure from this state. He appointed Dr Harriet L Hardy, Middlesex South, to this vacancy, announcing at the same time that Dr Hardy serves as physician to the Division of Occupational Hygiene in the Department of Labor and Industry.

The President announced his appointment of Dr Humphrey L McCarthy, Norfolk, Dr John J Dumphy, Worcester, and Dr Michael A Tighe, Middlesex North, as a committee to confer with Major General Hawley concerning the medical care of veterans.

He announced that he had appointed Dr Elmer S Bagnall, Essex North, Dr David Cheever, Suffolk, Dr Roger I Lee, Suffolk, Dr Charles E Mongan, Middlesex South, Dr Frank R Ober, Suffolk, Dr Walter G Phippen, Essex South, and Dr George Leonard Schadt, Hampden, as a committee to propose to the Council a director of medical information and education.

He further announced that, in accordance with the vote of the Council, he had appointed the Com-

mittee on Rural Medical Service to Confer with the Massachusetts Farm Bureau Federation as follows: Dr Joseph C Merriam, Middlesex South, *chairman*, John E Moran, Franklin, and Patrick J Sullivan, Berkshire.

He said, in accordance with the action of the Council at its special meeting held on January 9, 1946, he had appointed Dr Elmer S Bagnall, Essex North, principal, and Dr Leland S McKittrick, alternate, to appear before the appropriate committees of the Congress of the United States for the purpose of making known the views of the Massachusetts Medical Society with regard to Senate Bills 1318 and 1606.

Confirmation of these appointments were moved by Dr Leavitt. This motion was seconded by Dr Felton, and it was so ordered by vote of the Council.

#### NEW BUSINESS

Dr Arthur N Makechnie, Middlesex South, speaking for that district, asked that all the members of the Society be polled by postal card as to whether or not they favored the passage of the Wagner-Murray-Dingell Bill (Senate 1606). He said that such members be asked to answer "yes" or "no" and that they designate whether they are specialists or general practitioners. He expressed it as his opinion that such a poll would show 90 per cent in opposition. This matter was referred to the Committee on Legislation.

The following resolution, signed by Basil E Barton, secretary of the Norfolk District Medical Society, was offered:

As a result of a vote taken by a pre-Council meeting of the Norfolk District Medical Society, held on January 30, 1946, the following resolution was offered:

That it is the sense of the councilors of Norfolk District that a list of the final vote of the Massachusetts legislators on the Chiropractor Bill of 1945 be published in the *New England Journal of Medicine*. This list to be published by districts rather than alphabetically and, if space is difficult to obtain, that it be published in several successive issues, a few districts at a time.

This resolution was referred to the Committee on Legislation.

Dr James M Baty, Massachusetts Chairman of the American Academy of Pediatrics, read a communication (Appendix No 9) addressed to the president, officers and members of the Council of the Massachusetts Medical Society descriptive of a survey which the Academy is conducting as to the medical needs of the children of the United States and the facilities available to meet these needs.

Dr Baty moved that the Council rules be temporarily suspended so that he might ask for the immediate approval of the survey. The motion to suspend the rules was seconded by Dr Smith.

Dr Mongan asked for a restatement of the motion. This Dr Baty did.

Dr Mongan, in opposing the motion, said that all such business should come to the Council by way of the Executive Committee, that the proposition



## APPENDIX NO 2

## REPORT OF THE COMMITTEE ON FINANCE

The Committee on Finance met on December 12, 1945, at the Headquarters of the Massachusetts Medical Society, 8 Fenway, to discuss the budget of the Society for 1946. Present were Dr Charles F Wilinsky and the chairman of the committee, together with the secretary and the treasurer of the Society, Dr Michael A Tighe, and Dr Eliot Hubbard, Jr. Our report follows.

The Massachusetts Medical Society has come through the war years without a deficit, and indeed with a surplus each year. This has occurred despite lower income from membership dues, and despite the loss of \$4000 of expected profit from our annual meeting in 1945 because this meeting was not held. This surplus has varied in the past seven years from a low of \$4624 in 1938 to a high figure of \$18,335 in 1943. Investments in the General Fund (i.e., reserves) have been increasing, and now have reached the sum of \$167,614 as of December 31, 1944, exclusive of the Building Fund. Our surplus this year is estimated to be \$4042.44. Of this, \$2134.52 represents income from the Building Fund leaving a usable surplus of \$1907.92. (We end this year with a bank balance of \$12,807, December).

The budget of 1946 contains three items which promise to increase our income for 1946, as against 1945. The first item is membership dues. We anticipate \$45,000 from dues in 1946, compared with \$39,000 in 1945. It is possible we shall receive more, as our peak sum from dues has been as high as \$51,000. The second item is the Committee on Arrangements (for the annual meeting). We expect \$4000 from this source. The third item is the *New England Journal of Medicine*. The *Journal* expects to turn over to the Society after December 31, 1945, \$15,000 or more. This item represents a striking change in our budget. Instead of calling for sums of money from the Society varying from \$11,000 per year to lower figures in the past few years, the *Journal* has used none of the \$8000 allowed in our budget for 1945, and expects to turn over to the Society \$15,000 or more. This money can be treated as income for 1946 instead of reserves. The \$5000 allocated to the *Journal* in our budget for 1946 represents an emergency item and it is very unlikely that it will be used. We expect money to come from this source in the future, for the number of subscribers to the *Journal* and the advertising rates have greatly increased. The amount will vary. Expected increase in costs next year make the estimated profit for 1946 only \$6000 instead of the \$19,500 (ten months' operation) or more for 1945. The amount may well be larger.

The expense column of the budget shows some decreases, especially because of the discontinuance of the Committee on Military Postgraduate Teaching. However, the chief characteristic of the expense column is increased expenses. The chief increases lie in greater cost of sending delegates to the A. M. A. Convention, because of its being held in San Francisco, increase in the Secretary's and in administrative expenses, and increased expenses for educational courses for members and for the Bureau of Clinical Information. Not included in the budget is the salary of the projected Director of Information and Education and his expenses—a figure which may represent \$8000 to \$15,000. Without this item, our expenses next year are estimated at \$55,488. Allowing for the expenses of the new director our expense budget may be \$65,000 to \$70,000. Our income without money from the *Journal* is estimated at \$56,161. Should the *Journal* add \$15,000 to our income, we shall have adequate income to pay expenses, with perhaps a little for reserves. If the income from the *Journal* is \$6000 or less, as anticipated, we shall undoubtedly have a deficit in 1947. It is clear that our increasing expenses may soon result in a situation where the Society must decide how we shall raise money to meet them.

PEER P JOHNSON  
EDWARD J O'BRIEN  
CHARLES F WILINSKY  
FRANCIS C HALL, *Chairman*

## SUPPLEMENTARY REPORT

Since the meeting of the Committee on Finance and after this report and budget were drawn up, the Committee on

Legislation, through Dr Reginald Fitz, has reported that the number of bills before the Massachusetts Legislature is large and that the Committee on Legislation, therefore, may have unusual expenses.

It is important that sufficient funds be allowed in the budget to be used for legal counsel. We are therefore submitting this request for an additional \$2000 for the Committee on Legislation.

## EXPENSES FOR 1945 AND BUDGET FOR 1946

Budget 1945	Expenditures 1945		Budget 1946	Change
		Salaries		
\$1,000	\$3,000 00	Secretary	\$3,000	
4,000	4,000 00	Executive secretary	4,000	
2,000	2,000 00	Treasurer and assistant treasurer	2,000	
		Expenses of officers and delegates		
400	613 24	President	400	— 350
200	0	President-elect	200	
1,000	3,542 37	Secretary	4,184	+ 384
2,000	2,032 95	Treasurer	2,100	+ 400
500	0	Executive secretary	0	— 500
0	0	Supervising censors	0	
700	850 00	Delegates to House of Delegates (San Francisco)	3,000	+ 2,300
200	200 00	Shattuck Lecture	200	
400	400	Cotting Luncheon	500	+ 100
2,000	2,699 90	General administrative expenses (under supervision of president and secretary)	2,700	+ 700
		Committees elected by district societies		
400	343 39	Executive	500	+ 100
3,200	3,331 98	Legislature	3,350	+ 150
1,000	1,369 44	Public Relations	1,200	— 100
		Labor and Industry		
0	0	Public Information	0	
		Nominations	0	
		Standing committees		
200	230 43	Arrangements	200	
200	173 76	Ethics and Discipline	200	
20	20 00	Finance	25	
\$1,000	\$981 78	Medical Defense	1,500	
0	0	Medical Education	0	
100	86 17	Membership	150	+ 50
4,000	4,351 00	Society Headquarters	4,459	+ 441
10	15 14	Publications	20	+ 10
8,000	0	<i>New England Journal of Medicine</i>	5,000	— 3,000
1,700	1,693 86	Directory and miscellaneous	100	— 1,600
200	64 45	Public Health	300	+ 100
200	127 06	Industrial Health	250 00	+ 50
		Special committees		
0	0	Cancer	0	
50	0	Physical Medicine	0	— 50
50	0	Postgraduate Instruction	50	
0	32 83	Expert Testimony	50	
50	08	Tax-Supported Medical Care	50	
50	0	To Meet with Massachusetts Hospital Association	0	— 50
50	35 65	Maternal Welfare	50	
50	8 66	Rehabilitation	50	
1,000	685 84	Postpayment Medical Care	0	— 50
600	22 73	Military Postgraduate	0	— 1,000
1,200	578 95	War Participation	0	— 600
		Postwar Loan Fund	800	— 400
		Bureau of Clinical Information		
1,000	1,630 17	Postwar Planning	10,500	+ 2,200
1,500	0	(1) Co-ordinating Education (\$1,700)		
	0	(2) Hospitals		
	104 15	(3) Medical Economics		
	59 65	(4) Medical Schools		
	32 78	(5) Organization		
	1,532 20	(6) Postgraduate Medical Education (\$6,000 00)		
		(a) Bureau of Clinical Information (\$2,500)		
2,400	2,899 15	Council Rules	50	+ 50
1,000	0	Medical Advisory to OPA	0	— 10
0	0	To Meet with Industrial Accident Board	100	+ 100

Society would be acted on. The President said that the Committee on Legislation could act on it immediately. Dr. Kickham pointed out that, if the list as called for in the resolution is not published within the next few weeks, its publication will have no point.

The Secretary asked to have referred to the appropriate committee the question of the formation of a woman's auxiliary to the Massachusetts Medical Society, which shall be affiliated with the Woman's Auxiliary of the American Medical Association. The President referred the question to the Committee on Public Relations.

The following letter was read by the Secretary

MASSACHUSETTS HOSPITAL SERVICE, INC.  
MASSACHUSETTS MEDICAL SERVICE

January 18, 1946

Dr. Reginald Fitz  
319 Longwood Avenue  
Boston, Massachusetts

Dear Dr. Fitz:

At a recent meeting in Washington, we attempted to get pay-roll deduction for federal employees. Legislation will be required and a number of government officials suggested that a word of approval from the American Medical Association would be useful. I therefore suggest that appropriate action be taken by the Massachusetts Medical Society recommending approval of the principle of pay-roll deduction for federal employees that they may have Blue Shield and Blue Cross in the usual way. Such action should be transmitted to the American Medical Association to support appropriate action by that group.

I do not see how this can be at all controversial since it is much better to enroll federal employees on a pay roll deduction basis than by the present cumbersome collection basis. I would thank you very much for instituting appropriate action and I trust that it is quite in order.

Sincerely yours,

R. F. CARALANE  
Executive Director

This letter was referred to the Committee on Tax-Supported Medical Care of the Committee on Public Relations.

The Secretary read certain letters from Dr. Shields Warren. They were referred to the Committee on Public Relations.

The Secretary read a letter from the Greater Boston Medical Society. This letter was referred to the Subcommittee on Postgraduate Education of the Committee on Postwar Planning.

The Secretary read a letter relative to the observance of Social Hygiene Day. This letter was referred to the Committee on Public Relations.

Dr. Bagnall moved that the Council adjourn. This motion was seconded by Dr. Hornor, and it was so ordered by vote of the Council.

The President announced the Council adjourned at 1:50 p.m.

MICHAEL A. TIGHE, Secretary

## APPENDIX NO 1

### ATTENDANCE OF COUNCILORS

#### BARNSTABLE

C. H. Keene

#### BERKSHIRE

I. S. F. Dadd  
Solomon Schwager  
Helen M. Scoville  
P. J. Sullivan

#### BRISTOL NORTH

W. H. Allen  
J. H. Brewster  
J. L. Murphy  
W. M. Stobbs

#### BRISTOL SOUTH

E. D. Gardner

C. C. Tripp  
Henry Wardle

#### ESSEX NORTH

E. S. Bagnall  
R. V. Baketel  
Elizabeth Councilman  
H. R. Kurth  
P. J. Look  
G. L. Richardson  
F. W. Snow

#### ESSEX SOUTH

Bernard Appel  
H. A. Boyle  
R. E. Foss  
Loring Grimes  
A. E. Parkhurst  
E. D. Reynolds  
H. D. Stebbins  
C. F. Twomey  
C. A. Worthen

#### FRANKLIN

H. M. Kemp

#### HAMPDEN

J. L. Chereskin  
A. J. Douglas  
A. G. Rice  
G. L. Steele

#### MIDDLESEX EAST

J. L. Anderson  
Richard Dutton  
E. M. Halligan  
M. J. Quinn  
R. R. Stratton

#### MIDDLESEX NORTH

A. R. Gardner  
M. A. Tighe

#### MIDDLESEX SOUTH

E. W. Barron  
Harris Bass  
J. M. Baty  
J. D. Bennett  
G. F. H. Bowers  
Madelaine R. Brown  
R. N. Brown  
R. W. Buck  
E. J. Butler  
J. F. Casey  
C. L. Derick  
J. G. Downing  
H. Q. Gallupe  
V. A. Getting  
H. G. Giddings  
Eliot Hubbard, Jr.  
F. R. Jouett  
A. A. Levi  
A. N. Makechnie  
P. H. Means  
C. E. Mongan  
G. M. Morrison  
J. P. Nelligan  
E. J. O'Brien, Jr.  
Fabyan Packard  
Max Ritvo  
H. P. Stevens  
J. E. Vance  
C. F. Walcott  
B. M. Wein  
Hovhannes Zovickian

#### NORFOLK

B. E. Barton  
Carl Bearse  
D. J. Collins  
William Dameshek  
G. L. Doherty  
Albert Ehrenfried  
H. M. Emmons

J. B. Hall  
R. J. Heffernan  
I. R. Jankelson  
C. J. Kickham  
C. J. E. Kickham  
F. P. McCarthy  
H. L. McCarthy  
Hyman Morrison  
D. J. Mullane  
J. J. O'Connell  
W. R. Ohler  
H. C. Petterson  
D. D. Scannell  
J. A. Seth  
L. A. Sieracki  
Kathleyne S. Snow  
S. L. Skvirsky  
J. W. Spellman  
J. J. Walton  
N. A. Welch

#### NORFOLK SOUTH

D. L. Belding  
Harry Braverman  
Frederick Hinchliffe  
D. B. Reardon

#### PLYMOUTH

P. H. Leavitt  
C. D. McCann  
G. A. Moore  
B. H. Pearce  
W. H. Pulsifer

#### SUFFOLK

W. H. Blanchard  
W. J. Brickley  
W. E. Browne  
A. J. A. Campbell  
David Cheever  
Pasquale Costanza  
Reginald Fitz  
Maurice Fremont-Smith  
Joseph Garland  
F. C. Hall  
A. A. Hornor  
R. I. Lee  
W. J. Mixer  
Donald Munro  
H. L. Musgrave  
H. F. Newton  
R. N. Nye  
F. R. Ober  
J. P. O'Hare  
L. E. Parkins  
L. E. Phaneuf  
Helen S. Pittman  
W. H. Robey  
R. M. Smith  
J. J. Todd  
Conrad Wesselhoeft

#### WORCESTER

B. H. Alton  
A. W. Atwood  
George Ballantyne  
Gordon Berry  
F. P. Bousquet  
E. J. Crane  
J. J. Dumphy  
W. J. Elliott  
John Fallon  
L. M. Felton  
L. P. Leland  
W. F. Lynch  
R. S. Perkins  
O. H. Stansfield  
J. C. Sullivan  
R. J. Ward  
B. C. Wheeler

#### WORCESTER NORTH

C. B. Gay  
J. G. Simmons

## APPENDIX NO 3

## REPORT OF THE COMMITTEE ON PUBLIC RELATIONS

The Committee on Public Relations of the Massachusetts Medical Society desires to transmit to the Council of the Massachusetts Medical Society the following items

It is recommended by the Committee on Public Relations that a certain plan suggested by Dr Quimby Gallupe be approved by the Council of the Massachusetts Medical Society. This plan is as follows

For many years the Commonwealth of Massachusetts has registered to practice medicine a number of physicians who have been graduated from unrecognized medical schools. Henceforward, by legislative action, physicians with unapproved educational background no longer will be eligible for registration in Massachusetts. Such physicians who have been registered in the past, however, will continue to practice. They are the doctors of many families in the Commonwealth yet they may not be permitted to care for their patients in our hospitals. Such a situation may prevent patients from receiving as adequate medical care as they have the right to expect from the profession and it tends to encourage the flourishing of inferior hospitals. It is not for the public good. Therefore, the following proposal is presented

Let the trustees and staff of each licensed community hospital in Massachusetts that wishes to do so, be encouraged to invite all registered doctors of medicine in its community to a meeting. At this meeting let the following plan be announced. Henceforward, all such registered physicians in the community are to be invited to attend the hospital's staff meetings, ward rounds, and clinicopathological conferences. The hospital's laboratory and x-ray facilities are to be made available to them. The opinions of the active and consulting staff members are to be made available for consultation. Such physicians are to be invited to send their patients to the hospital under the care of the hospital staff. Their professional behavior is at first to be watched carefully by staff members who may come in contact with them and after a reasonable preliminary period of observation the courtesy privileges of the hospital may be made available to them under some such conditions as the following

At first, as members of the courtesy staff they will be privileged to care for their medical patients under staff guidance. They will not be permitted to do surgery or operative obstetrics until they can demonstrate that they have experienced satisfactory postgraduate training in these specialties or can prove, satisfactorily, their capabilities to the chiefs of these services. Their records will be carefully inspected. Their attendance at staff meetings and other conferences will be recorded. Their relations to their fellows and to their patients will be noted. Their full support of the community effort and their loyalty to the hospital will be expected. Eventually if their work proves satisfactory, they may hope to attain full staff membership.

Such a plan, to operate effectively, requires support of the trustees and the staff of each community hospital wishing to engage in an educational endeavor of this character. These bodies must appreciate that if their communities are to reap benefits from the plan, both trustees and hospital staff must work to perfect its details. The plan should be approved by the American College of Surgeons and the American Medical Association. To succeed, it requires support by the Massachusetts Hospital Association and by the Massachusetts Medical Society.

The Committee on Public Relations recommends that the Council approve this plan and take appropriate measures toward its activation.

## REPORT OF SUBCOMMITTEE ON TAX-SUPPORTED MEDICAL CARE

Your committee has received a letter from the Honorable Philip J. Philbin, congressman from the Third Massachusetts District and member of the House Committee on Military Affairs. Herein is stated "I am pleased to say that I believe that veterans ought to be able to receive treatment from doctors of their own choice and in hospitals of their own choice in their own communities as supplementary to their right to clinical and hospital care. I am looking forward to the statement of your committee on these

matter, and will gladly join with you in working for more constructive and more effective care and treatment of our beloved veterans."

The Council already has advocated free choice of physicians by veterans for their medical care. Your committee has studied this principle in greater detail. We reaffirm our belief that veterans can obtain most satisfactory and economical medical care by employing licensed physicians of their own choice and of their own communities in whom they have confidence. We believe that veterans requiring hospital care can best be cared for by hospitalization in licensed civilian hospitals of their own choice and particularly in licensed civilian hospitals in their own communities when such hospitals are available. We believe that the costs of home or office visits for veterans and their professional care in hospitals should be paid at the prevailing rates of each community for such services. We believe that the costs of hospitalization for veterans in local licensed civilian hospitals should be met by arrangements for this purpose between each of such said hospitals and the Veterans Administration. We believe that each district society should appoint a committee authorized to meet on call by the Veterans Bureau for the purpose of adjusting any disputes or difficulties that might arise under such a program.

Your committee has received a letter from Major General Paul R. Hawley, acting Surgeon General of the Veterans Administration of the United States of America, requesting that the Massachusetts Medical Society appoint a committee to confer with him about medical care of veterans. This was discussed by all members of the Committee on Public Relations. Dr. Ellison moved and Dr. Sullivan seconded the motion requesting that this committee be appointed immediately by Dr. Fitz because it was an emergency. This motion was carried unanimously. Dr. Fitz then appointed Dr. John J. Dumphy, Dr. Michael A. Tighe and Dr. Humphrey L. McCarthy to serve on such a committee.

The chairman and Dr. Hornor met with Mr. O'Hare, agent of the Board of Public Welfare for the City of Boston, to discuss ways in which the boards of public welfare, particularly that in Boston, could obtain help from the Massachusetts Medical Society. It was brought out that all recipients of old-age assistance are entitled to free choice of physicians and it is incumbent on the local boards of public welfare to see that this practice is followed and that the physicians are properly paid. Our conference with Mr. O'Hare and a later conference with the Commissioner of Public Welfare for the Commonwealth of Massachusetts, Mr. Tomkins, causes us to recommend that each district medical society appoint a committee to act in an advisory capacity with their local boards of public welfare in attaining the ends above mentioned.

The Committee on Public Relations recommends that this report be accepted and the recommendations contained in it be adopted, and that as it relates to the Veterans Administration a copy of it be sent to the Honorable Philip J. Philbin.

The Committee on Public Relations recommends to the Council that if, at any time, the Massachusetts Medical Society has recommended that the prevailing rate of fees be reduced for the care of tax-supported medical cases that this action be rescinded.

ALBERT A. HORNOR, Secretary

## APPENDIX NO 4

## REPORT OF THE COMMITTEE ON LEGISLATION

Since the last meeting of the Council your committee has been actively engaged through subcommittees in co-operation with subcommittees of the Postwar Planning Committee and of the Committee on Public Relations in drawing an appropriate report on national legislation to be presented to the Council. This report was acted on at the special meeting of the Council held on January 9, 1946.

Your committee has been studying methods for bringing to the district societies a sense of the importance of medical citizenship and realization that only by the active interest on the part of individual doctors can their knowledge and views receive as much consideration as they deserve by any legislative body. It appears difficult to interest the busy practitioner in such matters, yet to accomplish this is extremely important in times when legislation pertaining to public health is becoming increasingly popular.

0	0	Re Directors of Blue Shield	0
0	0	Re Revision of By-Laws	0
0	0	Re Farm Bureau and Rural Medical Services	0
0	25 00	To Appt Director of Medical Information and Education	300 + 300
4 000	4,000 00	Refunds to district medical societies	4,000
\$57 495	\$43,864 94		\$55,538 \$1,957 (less)

\*Late appropriation

†Under Postwar Planning Committee.

‡Based on expenses for 10 months and estimates for 2 months

## DETAILED EXPENSE ACCOUNTS

<b>Expenses of President</b>			
Newspaper	\$45 00		
Lunches	31 03		
Clerical	84 08		
Travel, clerical, telephone (Dr Bagnall)	418 31	\$578 42	
<b>Estimate for November and December</b>			
Clerical	\$25 00		
Dinners	10 00	35 00	
		\$613 42	
<b>Expenses of Secretary</b>			
Clerical	\$1,695 46		
Postage and mailing	128 56		
Printing	1,126 03		
Diploma tubes	41 88		
Stenographic report of meeting	390 00	\$3,181 93	
<b>Miscellaneous expenses</b>			
Telephone	\$62 72		
	97 72	160 44	
		\$3,542 37	
<b>Expenses of Treasurer</b>			
Printing	\$239 39		
Clerical	502 83		
Loomis and Sayles	970 23		
Accountants	315 00		
Premium on bond	37 50		
Safe-deposit box	18 00	\$2 082 95	
<b>General administrative expenses</b>			
General clerical	117 82		
Office supplies	1,226 21		
Printing	406 50		
Telephone	655 15		
Travel	294 22	\$2 699 90	
<b>Expenses of Executive Committee</b>			
Clerical	\$145 68		
Dinner meetings	107 71	\$253 39	
<b>Estimate for November and December</b>			
Clerical	30 00		
Dinner meetings	60 00	90 00	
		\$343 39	
<b>Expenses of Committee on Legislation</b>			
Salaries, legislative agent (lawyer) and other expenses		\$1 590 00	
<b>Supplies</b>			
Printing and postage	\$458 49		
Telegrams	395 99		
Legislative Reporting Service	180 16		
Clerical	233 89		
Meetings	292 80	\$1,561 33	
<b>Miscellaneous</b>			
Miscellaneous expense	\$25 65		
Legislative directors	20 00	45 65	
		\$3 196 98	
<b>Estimate for November and December</b>			
Dinners	\$60 00		
Clerical	75 00	135 00	
		\$3 331 98	
<b>Expenses of Committee on Public Relations and Subcommittees on Public Information and Labor and Industry</b>			
<b>Committee on Public Relations</b>			
Printing	\$244 05		
Clerical	74 86		
Dinner meetings	491 43		
Travel	23 00		
Estimate for November and December	100 00	\$933 34	
<b>Committee on Public Information (now discharged)</b>			
Reports	\$25 00		
Miscellaneous and telephone	31 44		
Expenses Dr Candler and Dr Bauer	47 57		
Printing	16 76		
Clerical	21 65		
Dinner meetings	248 73	\$391 05	

<b>Committee on Labor and Industry</b>			
Dinner meeting			\$5 13
			\$1 169 52
<b>Expenses of Committee on Arrangements</b>			
Clerical	\$132 98		
Printing and postage	37 45		
Estimate for November and December	60 00	\$230 43	
<b>Expenses of Committee on Ethics and Discipline</b>			
Clerical work (December 1944 paid, 1945)	\$20 47		
Lunches	35 69		
Clerical to November	82 60		
Estimated for November and December	35 00	\$173 76	
<b>Expenses of Committee on Medical Defense</b>			
Legal expenses ending June 30	\$381 78		
Legal expenses ending November 15	200 00		
Estimate for November and December	300 00		
Miscellaneous legal work	100 00	\$981 71	
<b>Expenses of Committee on Society Headquarters (estimated)</b>			
Rent	\$3,248 00		
Cleaning	234 00		
Electricity	231 00		
Telephone	138 00		
Clerical	300 00		
Miscellaneous	200 00	\$4 351 00	
<b>Expenses of Committee on Publications</b>			
Profit and loss account of			
<i>New England Journal of Medicine</i>			
	Actual 1945*	Estimated 1946	
<b>Revenue</b>			
Advertising	\$73 000 00	\$60,000 00	
Engraving	1 000 00		
Reprints	7 500 00	8,000 00	
Subscriptions	62,000 00	65,000 00	
Miscellaneous	1,500 00	1,500 00	
	\$145 000 00	\$154,500 00	
<b>Expenses</b>			
Publication of Journal	\$75,000 00	\$90,000 00	
Publication of reprints	6,000 00	6,500 00	
Office and other salaries	29,000 00	34,000 00	
Commissions, fees etc	7,000 00	8,000 00	
Office and sundry expense	7,500 00	10,000 00	
	\$124,500 00	\$148,500 00	
<b>Profit</b>			
Appropriation	19 500 00	6,000 00	
	\$48,000 00	\$5 000 00	
<b>Directory</b>			
Clerical	\$165 98		
Printing	1 499 50		
Postage	28 38	1,693 86	
<b>Expenses of Committee on Industrial Health</b>			
Clerical	9 39		
Meetings	42 67		
Estimate for November and December			
Meetings	70 00		
Clerical	5 00	\$117 06	
<b>Expenses of Committee on Military Post graduate Teaching</b>			
Luncheon and dinner meetings	\$143 77		
Clerical	392 07		
Estimate for November and December	150 00	\$685 84	
<b>Expenses of Committee on Postwar Loan Fund</b>			
Envelopes	\$184 14		
Clerical	43 96		
Printing	51 94		
Addressing	20 00		
Mailing	35 00		
Interest on loans	200 00		
Meetings	44 81	\$579 85	
<b>Expenses of Postwar Planning Committee and Subcommittees</b>			
<b>Postwar Planning</b>			
Clerical	\$381 65		
Printing, mimeography and postage	64 25		
Dinner and luncheon meetings	486 91		
Meeting with hospital trustees chiefs of staff and executives, June 20	503 86		
Telephone	15 50		
Hospital Directory	3 00	\$1,455 17	
<b>Subcommittees</b>			
Medical Economics	104 15		
Postgraduate Education	32 20		
Curriculum	59 65		
Medical Organization	32 78		
Bureau of Clinical Information (transferred to Subcommittee on Post graduate Education, May 1945)	2 399 15	\$4,083 10	
<b>Estimates for November and December</b>			
Clerical	\$100 00		
Postgraduate Education	1 500 00		
Bureau of Clinical Information	500 00		
Meetings	75 00	\$2 175 00	

\*Based on ten months' operation

†Not used

## APPENDIX NO 7

## REPORT OF THE COMMITTEE ON PUBLIC HEALTH

The Committee on Public Health has had two meetings, and a subcommittee one meeting. Dr Bagnall of the subcommittee will make a supplementary report on his study concerning legal restrictions of the sale of drugs dangerous to the public health.

President Fitz referred to our committee a letter from the American Epileptic League, Incorporated, asking him to give them a list of physicians in rural areas who are competent to care for epileptics — an increased number of such cases are expected as casualties from our armed forces.

After a discussion of the subject in which we had the advice of Dr William Lennox, it was voted to recommend to the Council that we circulate the profession with a letter concerning the importance of the knowledge of recent advances in the treatment of epilepsy and offering to forward such material as is available on the subject to those interested. Material for this letter is attached. (See below.)

President Fitz also referred to us a communication from a group of school executives, asking for a committee from the Society to formulate plans for the improvement of medical services to the schools.

After discussion of the problem during which we were joined by Dr Florence McKay, it was voted to appoint a subcommittee to study the deficiencies noted and recommend a remedy.

We hope these recommendations will be ready to be presented to the Council in May.

This report has one informational study by Dr Bagnall — a report of progress on a study to improve the medical services to the schools and a recommendation that the Council approve of the committee's sending a letter to all the physicians in Massachusetts offering to send literature on the latest advances in the treatment of epilepsy to those who are interested.

ROY J WARD, Chairman

\* \* \*

Dear Doctors:

The Committee on Public Health of the Massachusetts Medical Society is commissioned by the Society to foster the knowledge of the prevention and treatment of disease by any appropriate measures. Your committee believes that epilepsy is a condition in which definite advances have been made in recent years of which physicians throughout the Commonwealth might be better informed. These advances are of three sorts: first, use of the electroencephalograph for diagnosis and as a guide in treatment; second, the newer drugs, phenytoin (dilantin) sodium for grand mal and psychomotor seizures, and trimethoprim (tridione) for the petit mal triad; and third, social aids, looking toward better opportunities for education and employment.

Also looking toward the future, there are plans for the establishment in Boston of a diagnostic-training research center, which might aid doctors in the better handling of their epileptic patients.

The American Epilepsy League (a national lay organization, which has a substantial group of medical advisors and headquarters at 50 State Street, Boston) has offered to supply doctors of the Commonwealth with pertinent information on various aspects of epilepsy. Some articles are reprints from medical journals; others are written for popular consumption.

A list of the items that are at present available is enclosed. Please check those which you would like for yourself or for patients and return in the enclosed envelope. Material will be sent from the office of the League. Even if you are not interested, or see no epileptics, will you assist in the collection of data by answering the questions at the end. Any comments or questions will be welcome.

Sincerely yours,

COMMITTEE ON PUBLIC HEALTH  
ERNEST M. MORRIS  
GEORGE L. STEELE  
CONRAD WESSELHOEFT  
ROY J WARD  
ELMER S BAGNALL

## MATERIAL AVAILABLE ON THE SUBJECT OF EPILEPSY

- 1 "The Treatment of Epilepsy." Medical Advisory Board of League.
- 2 "Marriage and Children for Epileptics." *Journal of Human Fertility*.
- 3 "Petit Mal, Myoclonic and Akinetic Epilepsies and Their Treatment with Tridione." *Journal of American Medical Association*.
- 4 "The Ghost is Out of the Closet." Yahraca. Printed by Public Affairs Committee, New York.
- 5 "Woman without Fear." *Woman's Home Companion*.
- 6 "Employment of Epileptics." *Journal of Industrial Medicine*.
- 7 "The Epileptic: Who he is what he can be." *Journal of Rehabilitation*.
- 8 "Epilepsy the hopeful disorder." *Parents Magazine*.
- 9 "The Nurse and Her Epileptic Patient." *American Journal of Nursing*.

A single copy of each of the above will be sent without charge and additional copies at 10 cents each, with reduction for larger numbers.

The following can be purchased through the League

- 10 *Science and Seizures: New Light on Epilepsy and Migraine* W G Lennox. Harper and Bros. \$2.00
  - 11 *Convulsive Seizures: A manual for patients, their families and friends* Tracy Putnam Lippincott. \$2.00
  - 12 *Epilepsia: A journal printed annually which contains an abstract of the world's literature on the subject of epilepsy.* \$1.00 a year
  - 13 *The Falling Sickness: A history of epilepsy* Oswei Temkin. Johns Hopkins Press. 1945. \$4.00
- Type of practice — general — medicine — surgery — specialty  
Approximate number of epileptics seen in past twelve months: in office, in public clinic
- Comments \_\_\_\_\_

## APPENDIX NO 8

## REPORT OF THE COMMITTEE ON POSTWAR PLANNING

In accordance with the action of the Council on February 2, 1944, the committee recommends that the Council of the Massachusetts Medical Society suggest to the Committee on Education and Labor of the United States Senate and to other appropriate authorities, that the Federal Government establish a department of health and welfare with a secretary in the President's Cabinet under whom would be coordinated all important health and welfare programs exclusive of those of the Army and Navy, and that the Division of Health should be under the direction of a physician.

Consultations with a representative of the Board of Collegiate Authority resulted in a better understanding of the approval of hospitals to provide training for returned veterans. Various meetings have been held with hospital representatives consisting of superintendents and staff members, to consider increasing the opportunities for returning veterans in Massachusetts hospitals. Seventy-six hospitals have listed their needs for interns and residents at 8 Fenway.

The Subcommittee on Hospitals further reported on the conversations that had been held with Dr Johnson, secretary of the American Medical Association's Council on Medical Education and Hospitals on how approval for hospitals for internships and residencies could be expedited. The question was asked how far the Society could assist the Council on Medical Education and Hospitals. Also, Dr Westmoreland reported at the Beth Israel Hospital in Boston on further details relating to approval of hospitals. He reported that the Council on Medical Education and Hospitals of the American Medical Association would appreciate such help under qualified leadership. Dr Fitz, a member of this Council, confirmed that the Council on Medical Education and Hospitals is practically overwhelmed by requests from hospitals for approval all over the United States. Also, he believes that this council of the American Medical Association would appreciate the assistance of a committee from the Massachusetts Medical Society that would help expedite probationary approval of Massachusetts hospitals.

The committee recommends that in view of the postwar emergency, the Council of the Massachusetts Medical Society approve the principle of active co-operation with the Committee on Medical Education and Hospitals of the American Medical Association, and that the Massachusetts Medical Society, through an appropriate committee, offer its services to the Council on Medical Education and Hospitals, in the appraisal for provisional approval of hospitals. It is further recommended that a committee of five be appointed by the president of the Society to co-operate with the Council on Medical Education and Hospitals with this objective.

The work of the Subcommittee on Postgraduate Medical Education, including direction of the Bureau of Clinical Information and the conduct of postgraduate courses, has steadily increased. Up to December 12, two hundred fifty-two service doctors have registered at the Bureau of Clinical Information. During the last three months of this year postgraduate exercises have been held in sixteen towns and plans for 1946 provide for twenty-four exercises in each of the six circuits. Actually these twenty-four exercises will include a two-day session during which a team of three or four instructors will teach in three to five different places. In addition, the committee has established tentative programs of bi-weekly postgraduate exercises in Boston. Certain localities in the State have asked for further and more frequently conducted exercises.

Your committee is in the process of studying and digesting as quickly as possible the various bills pertaining to public health and the practice of medicine which will be introduced in the next session of the Great and General Court of Massachusetts.

Dr. Humphrey L. McCarthy, on December 12, 1945, submitted his resignation as chairman of the committee. His resignation was accepted with regret by his fellow members of the committee and by the President. He proved imaginative, energetic and hard working. Fortunately he retains membership on the committee so that his services to the Society are not lost. Sufficient time has not elapsed for a new chairman to be elected, a method of selecting the chairman used by this committee for many years in accordance with *Robert's Rules of Order*. This authority states that any standing committee, by a majority of its number, usually elects a chairman.

This report is submitted as an informational report.

REGINALD FITZ, Acting Chairman

## APPENDIX NO 5

### REPORT OF THE COMMITTEE ON CANCER

A meeting of the Committee on Cancer was held September 19, 1945. Improvement in diagnostic procedures and methods of educating the laity in the disease, cancer, throughout the Commonwealth, were discussed and would appear to be of interest to the Council.

Vaginal smears for the diagnosis of uterine cancer are now a routine procedure in many of the cancer clinics in all female patients. It is expected that this method of diagnosis will be adopted by all the clinics in the near future.

Cancer symposiums have been sponsored by the cancer clinics in several cities. These were conducted both in the afternoon and evening to afford an opportunity for more to attend. Speakers of recognized ability in cancer therapy and from the various specialties in practice have addressed these gatherings. The large attendance at these symposiums has been very surprising and the requests from the laity for more frequent educational meetings of this type have been most gratifying.

Instruction in cancer in the public schools of Massachusetts in many communities is now a part of the regular curriculum. The value of such instruction both to the school children and to their parents with regard to early recognition and early treatment of the disease is inestimable.

Lynn and Malden have quite elaborate programs of instruction in cancer in the schools. It is hoped that cancer statistics of these communities will be compiled in the future to evaluate the results as compared with other communities with less extensive programs. Instruction in cancer is now a part of the school curriculum in many communities in Montana, North Dakota, Minnesota, Wisconsin, Iowa, Michigan, Pennsylvania, Alabama, Ohio and New York. In some states an outline for school programs is furnished the schools by the state medical society.

The Committee on Cancer is of the opinion that instruction in the disease, cancer, in the public schools is a valuable method of publicity and indorses in principle making such instruction a part of the school curriculum. The method of instruction, we believe, should be determined by the school authorities of the communities.

ERNEST M. DALAND  
THOMAS J. ANGLEM  
ALLEN G. RICE  
CHANNING C. SIMMONS  
GEORGE A. MOORE, Chairman

## APPENDIX NO 6

### REPORT OF THE COMMITTEE ON MEDICAL DEFENSE

I have your communication from the American Policyholders' Insurance Company regarding writing an over-all group malpractice liability insurance policy for members of the Society. (See below.)

I have sent this letter to the two members of the committee available. Dr. Edwin D. Gardner, of New Bedford, sees no reason why this company should not be seriously considered but does not state definitely that he favors group

malpractice-insurance protection for the entire Society written by one company. The other member, Dr. William R. Morrison, is very distinctly opposed to the plan, saying that he believes our present system of free choice with protection given to the members not insured by our own attorneys is a satisfactory one.

When Dr. Bagnall was president of the Society, he suggested that the plan of protection for medical defense should be studied again and considered on a different basis from our present one. At this time, Dr. Guy Richardson, of Haverhill, had made a considerable study of malpractice insurance as it has affected men in that community particularly, and believed that a better system than the one we now use might be worked out.

I mention all of this because I think probably the time has come when the entire problem should be reviewed. It is perfectly true that the two insurance companies now writing most of the malpractice insurance in this state, although their rates are somewhat different, do an equally good job. I would suppose that the American Policyholders' Insurance Company would like the entire business instead of simply being allowed to write the insurance as the other companies do. It will be remembered that some years ago the company represented by Mr. George Crosbie, which now writes a great deal of the insurance, wanted to have complete control over the malpractice defense of the Society and this was not approved by the Council.

The argument in favor of one insurance company over another is their financial rating, or their ability to pay their obligations in the face of a bad financial period.

I have long felt that the Massachusetts Medical Society might undertake its own insurance plan but I can easily see that this would involve too much difficulty in many ways. It would be comparable to starting the Blue Shield or something of that nature, which, although a great success, required a tremendous amount of work and continued endeavor on the part of many members of the Society.

I think this question might be discussed at the next meeting of the Executive Committee to see whether or not the time has come when the problem of malpractice insurance should be reviewed. I would like very much to be relieved from any responsibility in this matter since I seem to have too many irons in the fire. I would be glad to give my advice to any committee appointed, to the best of my ability, but would prefer not to have to make the study myself.

ARTHUR W. ALLEN, Chairman

AMERICAN POLICYHOLDERS' INSURANCE COMPANY  
Home Office Boston, Massachusetts

November 17, 1945

Massachusetts Medical Society  
8 Fenway  
Boston, Massachusetts

Attention Secretary

Dear Sir:

The American Policyholders' Insurance Company, an American stock insurance company, is desirous of establishing for the Massachusetts Medical Society a group malpractice liability insurance policy for the members of your society who would want to subscribe to it. We would issue a master policy to the Society and individual policies to the members subscribing to it for whatever limits of liability they would desire, of course, only members of the Society in good standing would be eligible under this group arrangement.

We are in a position to offer this protection to your members at an exceptionally low cost. The protection would be all-inclusive and would insure the members of your society for any and all contingencies upon which a claim or suit for malpractice could be based.

If it is possible to discuss this matter in detail with the Executive Committee of your society or with that committee whose function it is to handle matters of this kind for your Society, the writer would be pleased to discuss the matter with them personally at your offices at a time convenient to you, giving the writer sufficient notice so that transportation arrangements might be made.

Very truly yours,

JOHN A. NOLAN  
Malpractice Division

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Physicians	1416
Hospitals	943
Army	548
Navy	283
Miscellaneous	209
Social service	36
Job counseling for veterans	52
Total	3489

The following have been included: Department of Education, State House, Lovell Hospital, Fort Devens, Camp Edwards, Chelsea Naval Hospital, Hingham Shipyard Dispensary, Boston Navy Yard Dispensary, Army Dispensary, First Army Command, Navy Unit at Vanderbilt Hall, Harvard Medical School Library, Boston University School of Medicine Library, Boston City Hospital Library, special departments at Boston City Hospital and Bureau of Information in New York City.

SOURCE OF PHYSICIANS' REQUESTS

Alberta	1
Baltimore	1

Boston	74
California	4
Canada	5
Chile	1
Connecticut	7
Cuba	1
Illinois	8
Iowa	3
Kentucky	1
Massachusetts	77
Michigan	4
Montreal	4
New York City	2
New York State	7
Ohio	1
Pennsylvania	3
Rhode Island	2
St. Louis	1
South Africa	2
Utah	1
Washington State	1
West Virginia	3
Total	214

The committee has submitted the following budget to the Finance Committee for 1946

Salaries and expenses of postgraduate instruction for twenty-four sessions	\$6,000
Clerical and printing	1,000
Bureau of Clinical Information (Salary — Miss Gaston, etc.)	2,800
Meetings	700
Total expenses	\$10,500

The demand for postgraduate instruction will be greater in 1946 than ever before. The success of the postgraduate assemblies held prior to World War II has led to consideration of their renewal. The Committee recommends that the Council approve the initiation of plans for a postgraduate assembly in 1946.

HOWARD F. ROOT, *Chairman*  
LEROY E. PARKINS, *Secretary*

## APPENDIX NO 9

### LETTER FROM DR. JAMES M. BATY

February 6, 1946

To the President, Officers and Members of the Council of the Massachusetts Medical Society, Gentlemen:

The American Academy of Pediatrics at its annual meeting in St. Louis in November, 1944, approved a plan to make a survey of the medical needs of the children of the United States and the facilities available to meet these needs.

The organizational work for this survey has been completed. Dr. John Hubbard, of Boston, has accepted the full time position of director of this work and now has an office at the Children's Hospital in Washington, D. C. The Children's Bureau and the United States Public Health Service are co-operating in making this survey and have assigned full time workers to assist Dr. Hubbard.

North Carolina was selected as the pilot state for the survey. The work was begun in North Carolina in November, 1945, and has been completed. The data obtained in this state have not been analyzed completely as yet. It is now planned to begin the survey in the individual states throughout the country; it is hoped within six weeks to two months.

The survey is entirely fact finding in nature and will attempt to determine the nature as well as the amount of health services being rendered to children by physicians, hospitals, clinics, social agencies and other organizations. An executive secretary will be appointed in each state to do the work in co-operation with Dr. Hubbard and the members of the American Academy of Pediatrics and with the assistance of local organizations that are willing to participate.

It is hoped that the results of this survey will be of value to the medical profession in general and to the American Academy of Pediatrics in particular in the formation of sound opinions and constructive criticisms relative to legislation aimed to improve the quality and distribution of medical care.

Respectfully submitted,

JAMES MARVIN BATY, M.D.  
State Chairman for Massachusetts  
American Academy of Pediatrics

## APPENDIX NO 10

### SUPPLEMENT TO REPORT OF POSTWAR PLANNING COMMITTEE

A review of the activities of the Bureau of Clinical Information of the Massachusetts Medical Society for the year ending December 1, 1945, shows that the *Bulletin* was distributed to various groups including hospitals, private physicians, medical officers of the Army and Navy and Veteran's Bureau, social-service departments, medical schools and so forth, to a total of 3489. A further analysis shows that the *Bulletin*, while mainly distributed in Massachusetts, was also sent by request to fifteen other states and four foreign countries and Canada. Requests for the *Bulletin* have been received from such agencies as the Massachusetts Department of Education, libraries of medical schools and Army, Navy and veterans' hospitals.

Since August, 1945, there have been 204 requests for data on refresher courses, residencies or locations. During this period and especially in the last several months, the office has been visited in increasing numbers by returning medical officers who wish to get information and to discuss their personal problems. In conjunction with the above activities of the Bureau, the secretary of the Bureau keeps the Bureau of Information of the American Medical Association informed as to changes in address and status of all members of the American Medical Association registered from Massachusetts. This is accomplished by a monthly report. All returning veterans are requested to fill out a form-sheet

giving the data in regard to their military service, present address and other pertinent facts, which is transmitted to the Directory Department of the American Medical Association. Another activity of the Bureau is advice and help in filling out forms in regard to eligibility under the G. I. Bill of Rights and related information of the Veterans Administration. Many requests have been received in regard to the Blue Cross and Blue Shield.

The requests that have come to the Bureau are of many types and varied in their scope, for example, a wife wanted to know where she could obtain extra red points for her anemic husband, there have been requests for lists of convalescent homes, a "good doctor for marriage problems" and a "good doctor for diabetes." A physician called to know the name of a film, and where it could be obtained, that was given at one of the meetings of the Society. There have been requests for information about openings for doctors' secretaries and requests from visiting doctors for information about operations and clinics. Often physicians, while in Boston, keep in touch with the Bureau for help in planning their time so that their stay is of the greatest value. Two physicians from Montreal come to Boston regularly for refresher work and plan their time according to the schedule of the *Bulletin*. A doctor from Calgary, Alberta, comes several times during the year and uses the *Bulletin* for his guide, and gets in touch with the Bureau for extra data. Two real-estate firms have been in touch with the Bureau, and as a consequence one service man found a good office location and home, which was formerly occupied by a doctor. A second home is now in the process of being bought by a serviceman. The servicemen express their gratitude for the *Bulletin*, as it helps them plan their refresher work. They say they could not get along without it. These are some of the ways and means in which the Bureau has been helpful to the servicemen.

An extremely important function of the Bureau, and one that will increase in importance, is the co-ordination of information concerning refresher courses and opportunities for attendance at clinics of the various medical schools, hospitals and private clinics. To promote this, conferences have been held and requests made for submission to the Bureau of Information of such data so that it is available when requests are made by individuals. A plan is under consideration for admission to certain clinics by card in order to prevent overcrowding and interference with small groups. We have in contemplation a plan whereby the hospitals and clinics may submit their clinical facilities under classified headings. Thus an applicant to the Bureau could be told at what hospital and at what time various types of clinics are held, although it must be kept in mind that such clinics are not always open to all physicians.

The above summary, plus a perusal of the detailed report below, shows that the Bureau of Clinical Information of the Massachusetts Medical Society has justified the wisdom of its sponsors. Its activities have grown in diversity each month, as has the quantity of information requested and dispensed. It is a real satisfaction to read the letters of gratitude that have been received from those who have consulted the Bureau. The demand for the Bureau's service has become increasingly widespread, this first year has naturally been one of an experimental nature, but it appears to be an activity that has well justified the effort and expense involved.

This report could not be concluded without a word of commendation to Miss Mary D. Gaston, secretary of the Bureau, who has made every physician and layman who has called feel that there is a personal interest in each and that time and effort expended in his personal problem is the function of the Bureau.

The activities of the Bureau are a part of the functions of the Subcommittee on Postgraduate Medical Education. Dr. Richard Ohler, chairman of the committee, has made excellent progress in organizing the respective areas of the Commonwealth for clinical postgraduate instruction as well as the lecture course for the Metropolitan Boston area, as published in the *Journal*. The Clinical Information Bureau activities are under the direction of Dr. Charles J. Kickham, a member of the Committee on Postgraduate Medical Education. Dr. Kickham has prepared the above information about the Information Bureau.

HOWARD F. ROOT, M.D., *Chairman*  
LEROY E. PARKINS, M.D., *Secretary*  
Postwar Planning Committee



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Total	3489

The following have been included: Department of Education, State House, Lovell Hospital, Fort Devens, Camp Edwards, Chelsea Naval Hospital, Hingham Shipyard Dispensary, Boston Navy Yard Dispensary, Army Dispensary, First Army Command, Navy Unit at Vanderbilt Hall, Harvard Medical School Library, Boston University School of Medicine Library, Boston City Hospital Library, special departments at Boston City Hospital, and Bureau of Information in New York City.

## SOURCE OF PHYSICIANS' REQUESTS

Alberta	1
Baltimore	1

Boston	74
California	4
Canada	5
Chile	1
Connecticut	7
Cuba	1
Illinois	8
Iowa	3
Kentucky	1
Massachusetts	77
Michigan	4
Montreal	4
New York City	2
New York State	7
Ohio	1
Pennsylvania	3
Rhode Island	2
St. Louis	1
South Africa	2
Utah	1
Washington State	1
West Virginia	3
Total	214

## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 32181

#### PRESENTATION OF CASE

A forty-eight-year-old machinery salesman entered the hospital after suddenly collapsing on the street.

The patient had been known to be hypertensive for fifteen years, but no record of his blood pressure was available. For four or five years before entry he had been on a reducing diet and had dropped from a maximum of 250 pounds to about 160 pounds. One month before admission he noted for the first time mild dyspnea on moderate exertion. At about the same time he developed a nonproductive cough, which was not relieved by sitting or standing. There was no previous history of headaches, vertigo, tinnitus, orthopnea, precordial distress or ankle edema. On the day of admission he felt well until evening when, while walking against a cold wind, he was suddenly seized with a tight feeling across the anterior chest, just as if his vest were too tight. At the same time he became increasingly weak, and finally his knees buckled under him and he collapsed. His sister brought him to the hospital in a taxicab.

Physical examination revealed a pale, emaciated, anxious, somewhat dyspneic man appearing both acutely and chronically ill. He complained of feeling hot and of having a dry mouth and a tight feeling in the chest. The skin was generally warm and dry, but the hands were cool and moist. When sitting up, the neck veins were distended and pulsating. There were moist, crepitant rales over the bases of both lungs. The left cardiac border was percussed 14 cm. to the left of the midsternal line. The sounds were regular. A Grade II systolic murmur was heard at the apex. The liver was thought to be enlarged. There was moderate pitting edema over the ankles. A right inguinal hernia enlarged to the size of a grapefruit on coughing. The fundi showed flame-shaped hemorrhages and moderate arteriosclerosis with arteriovenous nicking.

The temperature was 100.4°F, the pulse 130, and the respirations 34. The blood pressure was 230 systolic, 150 diastolic.

Examination of the blood showed a hemoglobin of 15 gm. The white-cell count was 13,000, with

84 per cent neutrophils. The nonprotein nitrogen was 52 mg. per 100 cc., the serum protein 5.9 gm. and the cholesterol 203 mg. The urine gave a ++ test for albumin, the sediment contained many hyaline casts. The specific gravity of two specimens was recorded as 1.016 and 1.022, respectively. The vital capacity was 1000 cc.

An x-ray film of the chest showed a cardiac shadow enlarged in all diameters. The lung roots and pulmonary markings were prominent. The costophrenic angles were obliterated by fluid. An electrocardiogram showed sinus tachycardia, at a rate of 150, a normal axis and a PR interval of 0.12 second. T<sub>1</sub> was inverted, T<sub>2</sub> and T<sub>3</sub> were low and upright, ST was elevated, and the T wave was upright in Leads CF<sub>1</sub> and CF<sub>4</sub>, with slight inversion in Lead CF<sub>3</sub>.

The patient was given morphine, digitalis, Mercururin and ammonium chloride, but this resulted in no diuresis or a lowering of the pulse or respiratory rate. He developed increasing respiratory embarrassment, cyanosis and peripheral edema, and his general status persistently disintegrated.

On the fourth hospital day the heart sounds remained good. The blood pressure was 110 systolic, 90 diastolic, with no variation in respiration. The scleras appeared slightly jaundiced, but a blood specimen taken on the following day showed a van den Bergh of only 1+ mg. direct and 19 mg. total.

On the fifth hospital day, the respirations became Cheyne-Stokes in character and the patient fell into a stupor. He was placed on continuous intranasal oxygen, but in his irrational state he succeeded several times in removing the nasal catheter and climbing out of bed.

On the sixth hospital day respirations gradually ceased.

#### DIFFERENTIAL DIAGNOSIS

DR. EDWARD F. BLAND. We are concerned with a man in the middle-age group with severe hypertension of long standing. There had occurred a significant decrease in his cardiac reserve for a month and then, without warning, he collapsed on the street, with a feeling of tightness in the chest, which seems a little more than just the discomfort from respiratory distress. Shortly after admission the patient was described as being in considerable distress. He had evidence in his peripheral circulation of venous stasis (distended neck veins), and subsequently the x-ray films showed signs of congestion in the lungs, as well as a big heart. There are one or two things at this point that we should like to know. Nothing is said about a gallop rhythm. Such should have been present, and perhaps a pulsus alternans. We should also like to know about the pulmonic second sound, which is usually accentuated with this degree of pulmonary congestion. He was obviously in a critical condition.

Of the laboratory aids we expect most help from the electrocardiograms. The first is as described in the record, but instead of finding evidence of left-axis deviation and T wave changes, such as one would expect with a large hypertensive heart and cardiac failure, no axis deviation is recorded and the T waves are low, with only a little elevation of the ST intervals in the precordial leads. There was a subsequent electrocardiogram, which is not mentioned in the abstract. It was taken on the next day and is essentially the same as the previous one, with possibly a little tendency to right-axis deviation, which is even more bothersome.

May we see the x-ray films? Dr. Lingley, did this patient have an obviously enlarged heart, as is stated in the record?

DR. JAMES R. LINGLEY. I have nothing to add to the x-ray report in the record. The heart shadow is greatly increased in size, but there is characteristic configuration. There is marked enlargement of all the pulmonary vessels on both sides, as well as hazy density in the medial portion of the lung fields, which is consistent with pulmonary edema. There is also fluid at both bases, more marked on the left than on the right.

DR. BLAND. You do not see any notching of the ribs?

DR. LINGLEY. No.

DR. BLAND. No evidence of pulmonary infarction?

DR. LINGLEY. No.

DR. BLAND. These films support the physical findings of heart failure of both the right and left sides. Does this suggest to you a rheumatic heart?

DR. LINGLEY. No, the shape of the heart does not suggest rheumatic heart disease.

DR. BLAND. The appearance of the electrocardiograms is disturbing and makes one wonder if rheumatic heart disease complicated the hypertension. If so, the heart should have been fibrillating, but it was not. I believe that we can discard that possibility. Do you see any calcification in the valves?

DR. LINGLEY. No.

DR. BLAND. So far as the remaining laboratory findings are concerned, the patient had a mild leukocytosis and a slight fever, but both might have been due to heart failure. Of the renal studies, the specific gravity should be noted. The specific gravity is sometimes helpful when one is considering the possibility of significant renal impairment in the presence of heart failure. The urine is usually concentrated in cases of heart failure and congested kidneys. If it is low, one is suspicious of considerable renal disease. In this case, the specific gravity is not suggestive of significant renal impairment. The cholesterol was normal. I suppose that it was determined in an attempt to appraise the renal function. There is one interesting laboratory finding, namely, the slightly elevated van den Bergh reaction. Whenever we see a patient with the

signs of heart failure who later develops jaundice, we begin to think about pulmonary infarction. On the other hand it occurs occasionally after a large myocardial infarct.

The subsequent course was unsatisfactory, in that the patient did not respond to the measures that usually relieve congestive failure unless some very serious underlying process is present. Such must have existed here, since he went progressively downhill, with a coincident sharp drop in blood pressure.

Was myocardial infarction responsible for his progressive unfavorable course? The electrocardiogram is not helpful and actually a little disappointing. On the other hand, when we add up the whole course of events, including the drop in blood pressure, the failure to respond to treatment and the seriousness of the underlying heart disease, I favor as a first choice a myocardial infarct, in spite of the absence of much pain. The second choice, which seems to me a little less likely, is that he had pulmonary infarcts. If present, I think that they were not primarily the cause of his fatal disease.

On the other hand, was this simply acute dilatation of a seriously weakened heart? The heart may dilate because of acute myocarditis from a variety of causes, — notably, rheumatic fever, diphtheria and acute nephritis, — but we have no reason to suspect such in this patient.

Did he have chronic vascular nephritis? The evidence pointing to the kidneys is not particularly convincing one way or the other. Certainly the patient had long-standing hypertensive vascular disease and, hence, probably an element of vascular nephritis. Whether the latter was sufficient to prevent his response to the measures that are usually satisfactory is difficult to say.

In conclusion, as a first choice I prefer myocardial infarction as the precipitating cause of this patient's final illness.

May I ask Dr. Sprague his opinion of these two electrocardiograms, both of which are essentially the same? They are surprisingly negative for a man who had had hypertension for fifteen years and eventually died of heart failure.

DR. HOWARD B. SPRAGUE. There seems to be some inversion in the T wave, the second one. If you want anything more to help in the diagnosis of myocardial infarction, I do not see it.

DR. BLAND. Would you object seriously to that diagnosis?

DR. SPRAGUE. I do not see how one can object. The statement that the pulse pressure did not vary with respiration makes one wonder if they were thinking about pericardial involvement. There was no friction rub. It might have been some unusual thing such as a ruptured coronary artery with hemopericardium.

DR. BLAND. It seems to me that one bit of evidence against a significant amount of cardiac tamponade,

if you want to go that far, is that there was a lot of blood in the pulmonary circuit according to the x-ray films. Therefore it would not appear that there was a process sufficiently constricting to have prevented the flow of blood into the heart.

DR SPRAGUE: There is nothing in the electrocardiogram to support a diagnosis of pericardial irritation.

DR TRACY B MALLORY: Dr Lerman, will you tell us the impression on the wards?

DR JACOB LERMAN: From the story we thought that this patient had had an acute coronary occlusion, which precipitated congestive failure. The thing that bothered us was his failure to respond to what we thought was adequate therapy. He continued to go downhill, coughing considerably, and developed marked Cheyne-Stokes respiration. There was no explanation for it except to assume that he had had a large coronary occlusion with cardiac damage.

#### CLINICAL DIAGNOSES

Hypertensive heart disease  
Myocardial infarction

#### DR BLAND'S DIAGNOSES

Cardiac infarction  
Hypertensive heart disease  
Cardiac failure

#### ANATOMICAL DIAGNOSES

Pericarditis, acute, fibrinous  
Cardiac hypertrophy, hypertensive type  
Nephrosclerosis, moderate  
Peptic ulceration of stomach and duodenum, acute  
Hydrothorax, bilateral  
Arteriosclerosis, aortic and coronary, slight  
Chronic passive congestion  
Hypertrophic arthritis of spine

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The autopsy showed several things, and I do not know how to put them together. The unexpected finding was an acute pericarditis. There was also considerable hypertrophy of the heart, the weight being 600 gm, but the heart was not particularly dilated. There was diffuse congestion of the lungs, and in places some evidence of old organizing bronchopneumonia. There was quite severe arteriolar sclerosis in the kidneys, such as one would expect with long-standing hypertension. The questions are: Why did he have pericarditis? What did the pericarditis have to do with the symptoms?

It was a fibrinous pericarditis, rather than the purulent one that accompanies bacterial infection. There are several types of nonbacterial pericarditis. It is a frequent finding with an infarct of the heart, but there was no infarct of the heart here. Fibrinous pericarditis is also quite frequent in patients dying

in uremia, but we have little evidence that this patient died with uremia, since the highest non-protein nitrogen was only 52 mg per 100 cc. The kidneys showed vascular involvement but not the extensive atrophy of the parenchyma that one would expect in a patient who had died of renal insufficiency.

There were some other incidental findings that are peculiar, and again I cannot explain them. There were multiple acute ulcers in the stomach and duodenum. Acute gastroenteritis is often observed in the uremic state, and it can also occur in cases of simple cardiac failure. This, however, looked more like peptic ulceration than the usual superficial changes that one sees in either uremia or cardiac failure. I cannot tie the ulcers into the picture. We recorded the primary cause of death as acute pericarditis, but I have no idea of its origin or etiology.

DR BLAND: What about the myocardium? Was there any evidence of myocarditis?

DR MALLORY: We could not find a thing wrong with it, except hypertrophy.

DR ALLEN G BRAILEY: Would tuberculous pericarditis do it?

DR MALLORY: There was no evidence of tuberculosis.

DR JAMES B TOWNSEND: Was there any fluid in the pericardium?

DR MALLORY: Only a moderate amount, but quite a lot of fibrin. It looked at autopsy like the pericarditis that one sees with uremia.

DR BLAND: Was there cardiac tamponade?

DR MALLORY: I do not believe that there could have been.

#### CASE 32182

##### PRESENTATION OF CASE

*First admission.* A sixty-three-year-old Italian woman entered the hospital complaining of dyspnea, nausea and vomiting.

The patient had been well until four months before admission, when she had a sudden attack of dyspnea, chills, a fever of 103°F and pain in the right posterior chest. The pain was constant, not related to breathing and lasted one week. After two more weeks she felt well enough to resume her work as a chocolate dipper but she still complained of some weakness and exertional dyspnea. One week before admission, while stooping over a kettle of chocolate, she suddenly felt weak and dizzy, as if she were going to faint. She sat down in a chair and felt better, but fifteen minutes later she became nauseated and vomited her breakfast. She was then brought to the Emergency Ward, where she appeared to be in no acute distress but did complain of a vague feeling of fullness and burning in the epigastrium, with radiation to the right chest and "up into the head."

In the past her health had always been good except for occasional bouts of acid eructations

Physical examination revealed an elderly woman in no acute distress. The lungs were clear, and the heart was not enlarged. The pulmonic second sound was slightly greater than the aortic. There was slight tenderness to deep palpation in the epigastrium.

The temperature was 99°F, the pulse 124, and the respirations 26. The blood pressure was 170 systolic, 92 diastolic.

Examination of the urine showed a +++ test for albumin. The blood showed a hemoglobin of 90 per cent and a white-cell count of 13,500. The non-protein nitrogen was 23 mg per 100 cc. An electrocardiogram was read as normal except for sinus tachycardia. An x-ray film of the chest revealed linear areas of increased density in the posterior portion of the right lower lobe and general enlargement of the heart. A gastrointestinal series was negative.

On the following morning the patient felt entirely well and was discharged.

*Final admission* (five days later). At home she continued to vomit almost everything consumed. She felt constantly nauseated and had frequent acid eructations, with the same type of epigastric burning radiating to the right chest and neck. She had also experienced some dyspnea even at rest, but had no orthopnea, ankle swelling, cough, fever or leg pain.

On physical examination the patient appeared acutely ill. She was breathing rapidly but was not orthopneic. The skin was warm and moist, and the lips were slightly cyanotic. The neck veins were distended and pulsating. The heart, lungs and abdomen were the same as on the previous examination. There was questionable bilateral calf tenderness, but Homans's sign was negative.

The temperature was 98°F, the pulse 85, and the respirations 40. The blood pressure was 100 systolic, 70 diastolic.

The blood and urinary findings were essentially similar to the previous results. A repeat electrocardiogram showed normal rhythm, at a rate of 105, with a tendency to right-axis deviation. The PR interval was 0.14 second. T<sub>1</sub> was upright, T<sub>2</sub> and T<sub>3</sub> inverted, Q<sub>1</sub> prominent, TCF<sub>1</sub> and TCF<sub>2</sub> inverted except for a few upright TCF<sub>3</sub> complexes, and TCF<sub>4</sub> upright.

The patient's condition grew steadily worse. On the second hospital day the temperature spiked to 103°F and remained elevated. On the third day a definite gallop rhythm was heard at the base of the heart. On the fourth hospital day a definite swelling of the right calf was found. She became more cyanotic, dyspneic and apprehensive. Femoral-vein ligation was considered, but the patient expired before preparations could be completed.

## DIFFERENTIAL DIAGNOSIS

DR SYLVESTER MCGINN. Perhaps we should start by seeing the x-ray films.

DR JAMES R. LINGLEY. There are two sets of films, taken nine days apart. At the first examination the heart shadow is slightly enlarged. There are some bands of density in the right midlung field that have the appearance of old scars, which could have been due to infarcts in the past or to a scarring process of any nature. The second set shows an increase of 1 cm. in the transverse diameter of the heart. The diaphragm is higher in position, however, and this can explain the slight increase in the transverse diameter of the heart. The left lung field is clear. The right shows an area of increased density in the region of the base of the upper lobe. This shadow is rather indefinite, but I think that whatever caused it appeared between the two examinations.

DR MCGINN. I have just been handed the electrocardiograms. The first one was described in the abstract as normal, but on looking at the tracing it is quite abnormal in that it has deeply inverted T waves in Leads 2 and 3, which makes quite a bit of difference in the summary of the case. It might have made a difference in its handling.

There are three types of presenting symptoms — shortness of breath, epigastric discomfort associated with nausea and vomiting and pain in the right chest radiating to the neck, which I interpret as having been due to diaphragmatic irritation with distribution of the pain through the phrenic nerve. The major findings in the case, however, are those of acute right ventricular strain. One week prior to the final admission, we know that she had severe shortness of breath, a feeling of fullness in the mid-epigastrium and tenderness on palpation over the liver area. I believe that that was due to acute hepatic congestion. Sometimes acute congestion of the liver can be extremely painful and simulate an acute abdomen. There is also a note that the pulmonic second sound was louder than the aortic, the reverse of what one would expect, particularly with a blood systolic pressure of 170. Then there was radiation of pain to the neck, which I referred to previously as probably having been due to diaphragmatic pleurisy.

On the final admission the patient had cyanosis, rapid breathing, distended neck veins and a fall of blood pressure. These findings are consistent with strain on the right ventricle. A gallop rhythm was heard at the base of the heart. If gallop rhythm is due to left ventricular dilatation it is usually heard at the apex. When heard at the base of the heart, it is likelier to be due to right ventricular dilatation, particularly if it is in the region of the pulmonary conus. That is not an unusual finding in cases of pulmonary embolism. Then there was a change in the electrocardiogram, in that some ex-

dence of right-axis deviation appeared, which is further evidence of right ventricular strain. Later on, she had some calf tenderness and preparations were made for ligation.

Diaphragmatic hernia may cause undue strain on the chambers of the right heart. It is unusual. If she had had a small diaphragmatic hernia it is possible that suddenly a large part of the stomach went through the diaphragm into the chest and caused an acute compression of the lung. In this case a negative gastrointestinal series was reported, and I think that this diagnosis can be ruled out on that basis, as well as the facts that she had had no previous history of diaphragmatic hernia and that it is an extremely rare condition. I\* reported one, and one other case has been reported in the literature. The symptoms in both cases were identical with those of massive pulmonary embolism.

That leaves us with acute cor pulmonale, the sudden distention and dilatation of the chambers of the right heart secondary to obstruction in the pulmonary circulation. The most frequent cause is acute pulmonary embolism. I believe that this patient did have a pulmonary embolus. I have confidence in the electrocardiogram and will have to make a diagnosis of coronary thrombosis on this tracing, even though the history is far from typical. There is nothing in the type of pain to make one think of coronary thrombosis, but we cannot get away from the first electrocardiogram, which shows no evidence of pulmonary embolism, but rather a coronary type of electrocardiogram consistent with posterior myocardial infarction due to occlusion of the right coronary artery. If that assumption is correct, she did have a previous coronary thrombosis. The incidence of pulmonary embolism and infarction in cardiac patients is so high that I believe they were also present in this case, coincident with coronary thrombosis.

DR DONALD KING: Do the x-ray films show evidence of old pulmonary infarction?

DR LINGLEY: There are scars in the right lung that are consistent with old infarcts. The shadow that appeared between the two examinations is consistent with a fresh infarct.

DR KING: You would expect to find evidence of old infarction?

DR LINGLEY: The x-ray findings are consistent with it.

\*McGinn, S., and Spear, L. M. Diaphragmatic hernia, presenting clinical picture of acute cor pulmonale. *New Eng J Med* 224:1014-1018, 1941.

DR. FRED ALEXANDER: Does Dr. Sprague think that the inverted T waves in Leads 2 and 3 can be interpreted as evidence of cardiac disease of long standing?

DR SPRAGUE: I think that they could, but this does not look like a case of that type. The patient had a systolic pressure of 170, with a low diastolic pressure.

#### CLINICAL DIAGNOSES

Pulmonary infarction  
Thrombophlebitis, right leg  
Myocardial infarction

#### DR MCGINN'S DIAGNOSES

Acute cor pulmonale  
Pulmonary emboli and infarcts  
Coronary occlusion (old)  
Thrombophlebitis, right leg

#### ANATOMICAL DIAGNOSES

Pulmonary embolism, massive, bilateral  
Pulmonary infarcts, multiple, healed  
Focal infarction of left auricle  
Mural thrombus, left auricle  
Thrombophlebitis, superficial femoral and popliteal veins of left leg

#### PATHOLOGICAL DISCUSSION

DR TRACY B MALLORY: The autopsy showed as the immediate cause of death a massive pulmonary embolus that filled the major branches of both the right and the left pulmonary arteries. We also found in the lungs a number of old scars, which were quite characteristic of healed infarcts. There was not, however, any marked degree of cor pulmonale, and no gross evidence of myocardial infarction was noted at autopsy. A small partially adherent thrombus was present in the left auricle. Sections were made through that auricle, and there were several microscopic areas of infarction in the auricular muscle. I am throwing Dr. McGinn a lifeline, but I am not sure that that explains the electrocardiogram. The major coronary arteries were in fairly good shape, with just a few widely scattered patches of atheroma. Ante-mortem thrombi were found in the superficial femoral and popliteal veins of the left leg. There can be little doubt that these represented the source of the pulmonary emboli, since the veins of the right leg were normal and the auricular thrombus was on the left side of the heart.

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## THE INADEQUACIES OF MEDICAL CARE

### IV THOSE CONCERNING ITS ADJUNCTS

GIVEN proper distribution and cost of high-grade medical care, little can be accomplished if the necessary adjuncts are lacking, such as well equipped hospitals, adequate nursing personnel and continued progressive research concerning disease.

As stated in one of the previous editorials, lack of hospitals and poorly equipped hospitals are two of the chief reasons why recently graduated physicians refuse to settle in rural districts and certain small cities. Such a situation usually exists because these communities cannot afford to create or maintain such facilities. No doubt this inadequacy would be lessened by proposed national

legislation to build hospitals in areas of demonstrated need (Hill-Burton Bill), but to ensure a high quality of medical care, it may be necessary to employ full-time or to subsidize chiefs-of-service who have been properly trained.

Even in the large cities in which, ten years ago, there was considered to be a superabundance of hospital beds, it is now almost impossible to obtain space even for the patient who becomes seriously ill. This condition has chiefly resulted from two causes. In the first place, physicians and laymen have become aware of the fact that a moderately or critically ill patient can be cared for far better in a modern hospital than in the home, secondly, the widespread and enthusiastic support of Blue Cross plans has greatly increased the number of persons who, when ill, seek hospitalization. Obviously, to meet this demand present hospitals must be enlarged and new hospitals must be built, but some relief would result if better use were made of existing facilities—for example, hospitals could be placed on a seven-day week and rules limiting the period of convalescence could be enforced. The latter might be assisted by the creation of affiliated convalescent departments or homes.

For many years standards for the approval of hospitals, both regarding equipment and personnel, have been set by the Council on Medical Education and Hospitals of the American Medical Association and by the American College of Surgeons. More recently, certain states, including Massachusetts, have designated minimum requirements for approval by the appropriate state department. All this has resulted in a tremendous improvement in hospitals, but a great number are still substandard because they are either poorly equipped or inadequately staffed, or both. Further improvement seems to rest solely in state regulation, but the administrative boards and officers of nonprofit institutions could do a great deal to correct existing faults.

For hospitals in rural districts and small cities, the adoption of a plan similar to that sponsored by Bingham Associates Fund seems distinctly worth while. Under this scheme, consultative clinical and laboratory services, as well as opportunities for continued professional and technical training, are

available to numerous community hospitals in Maine through their affiliation with hospitals in two relatively large cities, Lewiston and Bangor, the latter, in turn, being affiliated with a large teaching unit, the New England Medical Center, in Boston

Lack of nursing personnel is another contributing factor to inadequacy of medical care. During the war, this scarcity was to be expected, although there seems to be no doubt that the armed forces demanded and obtained more nurses than they knew how to utilize. There appears, however, to be reason for believing that the shortage will continue, inasmuch as many of these nurses, having realized the advantages of relatively well paid and secure jobs, are loath to request discharge. Whether a sufficient number of young women can be induced to enter the nursing profession is doubtful, but an increase in facilities for the training of attendant or practical nurses would do much to relieve the present shortage. For this type of training the preliminary requirements are less demanding and the training period is of shorter duration than is the case with regular training schools, on the other hand, the young women who graduate are usually qualified to give routine care in hospitals, convalescent homes and private homes. Massachusetts and seventeen other states have already established schools for the training of attendant nurses, and have created boards for their licensing, and a nation-wide adoption of such a program would be advantageous.

Medical care cannot improve, all other things being equal, unless it receives the continued benefit of research in the cause and treatment of disease. Although a great deal was accomplished by relatively inco-ordinated research prior to the war, the advances made under the supervision of the Committee on Medical Research of the Office of Scientific Research and Development leave no doubt concerning the advantages of integrated investigation. Furthermore, efforts should be directed toward the diseases that are chiefly responsible for crippling and death, such as arthritis, cardiovascular diseases and cancer. As an example of the inconsistencies in the latter regard, it should be noted that the National Foundation

for Infantile Paralysis was able to raise over \$16,000,000 in 1945, whereas the American Cancer Society could only obtain about \$4,000,000. Finally, it should be borne in mind that, with taxation as high as it is at the moment and little probability that it will be appreciably reduced in the near future, contributions from individuals and groups for the furtherance of medical research will necessarily grow smaller and smaller. For these reasons proposed national legislation for the promotion and support of scientific research (Kilgore and Magnusen bills) seems not only proper but indispensable.

The practicing physician has little or no control over most of the above adjuncts of medical care, but all of them have a lot to do with the health of the people and all schemes aimed at improvement should receive the enthusiastic and energetic support of the medical profession.

#### H R 5296

MRS CLARE BOOTHE LUCE, Representative of the 4th Connecticut District, has introduced in the House of Representatives a bill notable in two respects: it recognizes an extra burden that is almost implicit in the practice of the health arts, and it is, pleasantly, one of the shortest documents of its nature that we have yet had the privilege of reading.

The full text of H R 5296 is as follows:

*Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled* That section 23-q of the Internal Revenue Code is amended by adding the following new paragraph, to read as follows:

"(4) That commencing with the taxable year 1941 physicians, surgeons and dentists shall be allowed an additional credit as a deduction on their income tax equivalent in terms of percentages to that portion of their time each year which is devoted to charity, free clinic work, and/or public research work,

"(5) The Commissioner of Internal Revenue shall prescribe by regulation the method of computing such time and the proof which shall be required in substantiation thereof."

This bill of the Connecticut congresswoman is obviously, a mere outline, an earnest of a good intention of which the practical details, if it should receive favorable consideration, would require amplification and interpretation. We have no idea of the reception that the bill will receive at the hands of the Committee on Ways and Means.



which it has been referred, but it is heartening to have a lawmaker take sympathetic recognition of the fact that medical practice is one of the most generous and unselfish branches of public service.

In strict interpretation, we imagine, of that which the doctor's daily life suffereth long and is kind, which envieth not, vaunteth not itself and is not tied up, may prove to be a problem for the Commissioner of Internal Revenue. May he have faith and may we have hope if such an opportunity presents his way! In the meantime, those who approve of this measure should communicate their interest to some member of the Committee on Ways and Means.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### LIMITED SUPPLY OF IMMUNE SERUM GLOBULIN

The current measles epidemic has created an unprecedented demand for immune serum globulin, which threatens to exhaust the available supply. Physicians are therefore urged to limit their use of this product to cases in which the need is clearly indicated, and to select modification rather than temporary protection, unless protection is definitely required. Temporary protection against measles can usually be obtained in exposed susceptible persons by administering 0.1 cc. globulin per pound of body weight (but not over 10 cc.) within the first six days after exposure. It is recommended for infants from six months to two years old and for older children who are debilitated, ill or faced with an emergency, such as travel or surgery. The protection so obtained does not last more than about three weeks.

Modification is desirable in other exposed susceptible persons, and may be obtained by giving 0.025 cc. per pound of body weight (equivalent to 1 cc. for a 40-lb child) within six or seven days after the date of exposure. Modified measles usually results in permanent immunity.

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Waverhill	May 1	William T. Green
Lowell	May 3	Albert H. Brewster
Salem	May 6	Paul W. Hugenberger
Brockton	May 9	George W. Van Gorder
Worcester	May 17	John W. O'Meara
Pittsfield	May 20	Frank A. Slowick
Springfield	May 21	Garry deN. Hough, Jr.
Fall River	May 27	David S. Grice
Hyannis	May 28	Paul L. Norton

Physicians referring new patients to clinics should get in touch with the District Health Officer to make appointments.

## CORRESPONDENCE

### A MISSTATEMENT

To the Editor: There recently appeared in the newspapers of Boston a statement, made by ex-representative Niland, of East Boston, before a legislative hearing at the State House, that the Health Commissioner of Boston was a graduate of the College of Physicians and Surgeons, of Shawmut Avenue, Boston.

This is absolutely untrue, since I graduated from Harvard Medical School in 1903, with postgraduate work at the Rotunda Hospital, Dublin, Ireland, in 1903-1904.

Except for several years during World War I and World War II during which time I served with the United States Navy, I have been associated with the Boston Health Department since September, 1904, in various positions.

I have also attended the public-health schools of both Harvard and Johns Hopkins.

FREDERICK J. BAILEY, M.D.  
Health Commissioner

Health Department  
Haymarket Square  
Boston 14

## BOOK REVIEWS

*Endocrinology of Woman* By E. C. Hamblen, M.D. 4<sup>th</sup>, cloth, 571 pp., with 157 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$8.00.

This book is divided into five parts.

Part one deals with the endocrine glands—their history, embryology, anomalies, anatomy, histology, secretory control, chemistry, physiology and interrelations. Following the introductory chapter, separate chapters are devoted to the thyroid gland, the adrenal glands, the pancreas, the parathyroid glands, the ovaries, the testes, the pituitary gland, the pineal gland and the thymus. The author justifies the inclusion of the testes in this presentation on the basis "that detailed knowledge of this gland is necessary for any real orientation of the problems of intersexuality, androgen therapy of woman, virilization syndromes and sterility."

Part two is concerned with applied endocrine physiology and discusses in detail antenatal growth and sexual differentiation, childhood development, sexual maturation, sexual maturity (menstruation, conception and gestation) and sexual regression.

Fifty-seven pages, comprising the third part, are devoted to endocrine diagnostic methods. This portion of the book is well illustrated and covers all the known clinical methods of endocrine diagnosis. The laboratory procedures useful in the diagnosis of normal and abnormal levels of endocrine function are alluded to, the normal values are emphasized throughout, so that abnormal values may be more easily recognized.

In part four the various functional disorders of the endocrine glands are discussed, and the effect of these glandular diseases on the sexual and reproductive functions of woman is stressed.

Part five contains eighteen chapters on endocrinology applied to gynecologic disease, and deals with such subjects as abnormal skeletal growth, abnormal sexual differentiation, obesity and leanness, abnormal uterine bleeding, functional uterine bleeding during adolescence, functional uterine bleeding during the childbearing age, dysmenorrhea, dermatologic abnormalities, cyclomastopathy, menstrual headaches and other cyclic syndromes, complications of pregnancy, complications of the puerperium, the incidence and causes of sterility, diagnostic methods in cases of sterility, the treatment of sterility, tumorigenesis, complications of the climacteric and commercial endocrine preparations. Only those commercial endocrine preparations with which the author is familiar are listed, but it is stated that omission of preparations from this list does not imply their inferiority.

The complex material of endocrinology of woman, well presented in this book, makes interesting reading. The illustrations are original, numerous, well chosen and clearly executed. Considerable material is condensed in tables throughout the text and the extensive bibliography at the conclusion of each chapter represents a compendium of the literature on the subject.

*The 1944 Year Book of Industrial and Orthopedic Surgery*, Edited by Charles F. Painter, M.D. 12<sup>th</sup>, cloth, 452 pp., with 282 illustrations. Chicago: The Year Book Publishers, 1945. \$3.00.

The editor has again compiled a most readable year book. He summarizes in a sufficiently descriptive but yet concise

manner the pertinent, reported happenings in the field of orthopedic surgery and industrial medicine. He has skillfully avoided the Scylla and Charybdis of most year books—a book that reads like a catalog or a volume that is so prolix that the reader yawns before the paragraph is completed. There is a definite place for a skillfully written synopsis and logically arranged index of the year's significant contributions in this field. Every reader will doubtless be disappointed at the absence of certain current papers that he, the reader, considered of value. The author's selection of papers, however, has been good. This volume should be of great aid to the busy surgeon in keeping abreast of current happenings in orthopedic surgery.

*Shoulder Lesions* By H. F. Moseley, M.A., D.M., M.Ch. (Oxon.), F.R.C.S. (Eng. and Can.) 4<sup>th</sup>, cloth, 181 pp., with 70 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$4.50.

The author has summarized in a concise and attractive manner present-day knowledge of disabilities of the shoulder. In doing this he has drawn on his wide experience in treating these lesions both in London and in Montreal. He shows how pitifully inadequate is modern knowledge of shoulder function and its disturbances. There are numerous well chosen illustrations. Chapters on x-ray interpretation and x-ray treatment and on operative procedures are included. Treatment is discussed in sufficient detail. A useful chapter giving thirty-one illustrative case histories completes the book.

Although no orthopedic surgeon will agree in toto with the author's conclusions, the sensible approach and the careful analysis of these lesions will meet with general approval. It can be recommended heartily as a readable and helpful book for all those interested in such disabilities.

## NOTICES

### ANNOUNCEMENTS

Dr. Edward A. Edwards announces his return to Boston at 374 Marlboro Street, his practice being limited to surgery, with special interest in peripheral vascular disease.

Dr. L. Robert Weiss, having returned from active service with the United States Army, has resumed the practice of allergy at 483 Beacon Street, Boston.

Dr. Ralph H. Wells announces his return from military service and the reopening of his office for the general practice of medicine at 1430 Massachusetts Avenue, Lexington.

### JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9-10 a.m.

#### MEDICAL CONFERENCE PROGRAM

Friday, May 3 — Clinical Diagnosis of Patent Ductus Arteriosus. Dr. Samuel A. Levine.

Wednesday, May 8 — Fluorine and Dental Caries. Dr. Basil G. Bibby.

Friday, May 10 — Psychotherapeutic Opportunities for the General Practitioner. Dr. Erich Lindemann.

Wednesday, May 15 — Silent Chest Lesions. Dr. Richard H. Overholt.

Friday, May 17 — Clinicopathological Conference. Drs. Stanley Bradley and H. E. MacMahon.

Wednesday, May 22 — Hyperadrenocorticism. Dr. Robert H. Williams.

Friday, May 24 — Application of Radioactive Iodine in the Treatment of Graves Disease. Dr. Saul Hertz.

Wednesday, May 29 — War Experiences in Abdominal Surgery. Dr. Charles S. Welch.

Friday, May 31 — The Role of Infection in Shock. Dr. Joseph C. Aub.

On Tuesday and Thursday mornings, Dr. S. J. Thannhauser will give medical clinics on hospital cases. On Saturday mornings, clinics will be given by Dr. William Dameshek. Medical rounds are conducted by some of the staff members from 12:00 to 1:00 in the Lecture Hall.

All exercises are open to the medical profession.

### BOSTON UNIVERSITY SCHOOL OF MEDICINE ALUMNI ASSOCIATION

The annual alumni reunion and continuation course Boston University School of Medicine will be held on and Saturday, May 10 and 11.

The continuation course will be held in the auditorium of the medical school this year, because its popularity has made more spacious accommodations necessary. There will be a nominal registration fee of \$1.00 for each of the three days.

On Saturday, May 11, at 6:00 p.m., in the Georgian Room and Parlor A, Hotel Statler, there will be a reception for the faculty members. At 7:00 p.m. there will be the annual dinner and banquet. The speakers will include President L. Marsh, Dean Donald G. Anderson, Dr. Reginald H. Wick and the speaker of the evening, Dr. James R. Miller of Hartford, Connecticut. Dr. Miller is going to speak on the topic "The National Health Program of the American Medical Association." Dr. Miller is a member of the Board of Trustees of the American Medical Association, and president of the New England Surgical Society. The tickets will be \$7.00 each. Dress is optional.

### NEW ENGLAND PEDIATRIC SOCIETY

The Spring meeting of the New England Pediatric Society will be held on Wednesday, May 15.

A day of clinical activities will be presented by Dr. M. Butler and members of his staff at the Massachusetts General Hospital. Dr. Edwards A. Park, professor of pediatrics, Johns Hopkins Hospital, Baltimore, Maryland, will be the speaker following the dinner.

### NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The spring meeting of the New England Obstetrical and Gynecological Society will be held in Worcester on Friday, May 29, with headquarters at the Wachusett Club.

### AMERICAN CONGRESS OF PHYSICAL MEDICINE

The twenty-fourth annual scientific and clinical sessions of the American Congress of Physical Medicine will be held September 4 to 7, inclusive, at the Hotel Pennsylvania, New York. Scientific and clinical sessions will be given each day. All sessions will be open to members of the medical profession in good standing with the American Medical Association. In addition to the scientific sessions, the annual institute courses will be held September 4, 5 and 6. These courses will be open to physicians and to therapists registered with the American Registry of Physical Therapy Technicians.

For information concerning the convention and instruction course, address the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2.

### SOCIETY MEETINGS AND CONFERENCES

#### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MAY 9

FRIDAY, MAY 10  
\*10:00 a.m. - 12:00 p.m. Medical Staff Rounds. Peter Beaty, M.D., Boston City Hospital.

12:00 p.m. - 1:00 p.m. Clinicopathological Conference (Boston City Hospital). Joseph H. Pratt, Diagnostic Hospital.

MONDAY, MAY 13  
\*12:00 p.m. - 1:00 p.m. Clinicopathological Conference. Peter Beaty, M.D., Brigham Hospital.

TUESDAY, MAY 14  
12:00 p.m. - 1:00 p.m. Dermatological Service. Grand Rounds. Dr. Dowling, Building Boston City Hospital.

\*12:15 - 1:15 p.m. Clinicoroentgenological Conference. Peter Beaty, M.D., Brigham Hospital.

WEDNESDAY, MAY 15  
\*10:30 - 11:30 a.m. Medical Clinic. Isolation Building. Amphlett, M.D., Children's Hospital.

(Notices continued on page xix)

# The New England Journal of Medicine

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Number 19

## A VISIT WITH OSLER\*

REGINALD FITZ, M D †

BOSTON

THOSE of us who were house officers at the Massachusetts General Hospital during the summer of 1910 will remember that the weather seemed continuously hot and that a great many citizens appeared to have typhoid fever. The medical wards were filled with the disease, during June, July and August we grew almost too familiar with its looks and with the dire manifestations of hemorrhage or perforation. But there were compensations: our sickest patients somehow often managed to grow well, not all hemorrhages were fatal, occasionally our surgical colleagues would sew up a perforated intestine and make us realize the miracle of modern surgical skill, and certainly we learned a great deal about an important infection.

August 25 was a particularly hot day. Even the newspapers commented on the high humidity, and we who were due to work in town over the week end read a little enviously about some of our more fortunate friends who were in the country indulging in the frivolities of tennis or golf. But on that day we had one reward that more than made up for the heat and our worries. Dr Osler accompanied the visit.

The East Medical Service by tradition is always justifiably proud — proud of its history, of the names on its roster, of the manner in which it does things. At that particular time Dr F Gorham Brigham was senior, Dr William S Parker was "pup," and I was junior. During the previous four weeks we had been exposed to a new experience. Our regular visiting man, Dr James J Minot, had turned over the service to Dr Joseph H Pratt. He was then a relatively new importation from Johns Hopkins and seemed fairly to bristle with ideas and energy, among other accomplishments he had gone so far as to introduce the interesting novelty of dictating notes on some of the cases so that our records had in his own words exactly what he thought of them. By and large, to make rounds with him proved an exciting adventure.

On that morning the visit started as usual. We were upstairs in Ward 30 and according to custom

had started to move around in clockwise manner when in blew Osler †. He came unannounced and unexpectedly. There was no need for any introductions, since Dr Pratt knew him well and we house officers had heard him speak at the Harvard Medical School on a memorable occasion during the preceding year, so that we were familiar with his appearance — his short figure, his mustache, his keen eyes. Now we were at once delighted by him — in part, perhaps, because to have a distinguished visiting professor from England was by no means a usual happening, even for the East Medical Service, chiefly, because instead of observing the amenities by commenting on the weather or the state of our health, he immediately became part of us by asking, "What have you got here?"

Here was a young woman who had just been transferred from the surgical ward. She had entered the hospital for the removal of a fibroid; everything had gone smoothly for fifteen days, when she was suddenly seized with pain over the right lower chest and with dyspnea and fever. On physical examination, when we first saw her, her heart seemed a little displaced outward, and at the right base below the angle of the scapula was an area of dullness, with distant bronchial breathing and voice transmission that sounded unusually close to the ear. We believed that she had a pulmonary infarct. Dr Brigham, whose privilege it was to present to the visit each morning the patients with their histories and physical findings, asked Dr Osler what he thought of the situation. Osler did no more than demonstrate the technic of palpatory percussion by tapping the young woman's back with all the fingers of one hand, and having done so said, "The resistance is quite marked, isn't it?" Dr Pratt, recalling Oslerian teaching of the importance of increased tactile resistance in the recognition of hydrothorax, asked if he thought the patient had a collection of fluid in her chest. Dr Osler was noncommittal, all he would say was that the resistance was striking, and finally that it might be well to insert a needle.

\*From the East Medical Service of the Massachusetts General Hospital.  
†Lecturer on the history of medicine. Harvard Medical School.

†Dr Pratt gives a somewhat different account of Dr Osler's visit.  
*Boston M & S J* 196 83 89, 1927.

Dr Brigham performed this operation on the following day and removed 400 cc of fluid. The patient subsequently developed a recognizable phlebitis in the left leg and later in the right leg, and in the course of time made an uneventful recovery. None of us have forgotten the skill with which Dr Osler demonstrated so nicely one of the essential signs of fluid, nor the tactful manner in which he suggested its removal.

The next patient had come to the hospital a week before because following a curettage she had begun to lose weight and strength, had become increasingly pale and had finally developed purpuric spots over both lower legs. On physical examination she proved to be feverish and to have a loud murmur at the precordium and a palpable spleen. She was markedly anemic and her blood culture was positive for what the bacteriologists regarded as an atypical pneumococcus. For want of any better treatment she had been given 5 gr of potassium iodide three times a day, and forty-eight hours later we observed that a painful, peculiar-looking bullous eruption had developed on her face and arms.

When Dr Osler noticed the rash, he sat down in a chair by the young woman's bedside and apparently paid no attention to her infectious endo-

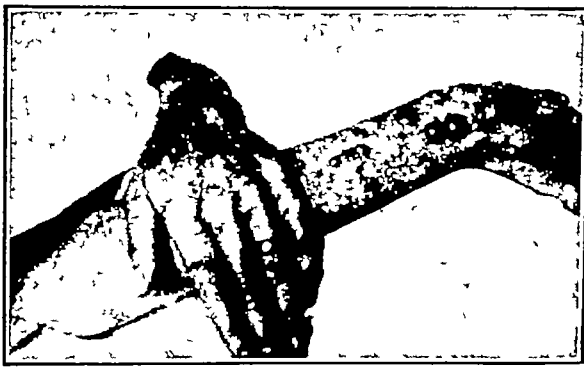
medical literature as was he. And I suspect that he began by telling us that here was something curious in the medical line. He may have reminded us of that little known periodical *The New York Medical Gazette and Journal of Health* and of the paper in it by Dr John O'Reilly — almost invariably misspelt O'Reilly — entitled "On the Effects consequent on the Administration of Iodide of Potassium, illustrated by cases," which appeared in January, 1854. For this makes pleasant reading and tells almost the whole story.

When a patient has been taking Iodide of Potassium for some days — probably on account of some peculiarity in his constitution — he is suddenly attacked with symptoms of fever, and almost contemporaneously with this disturbance of his system, will be observed on his forehead and face spots, varying in size and irregular in form, of a dark red color. As the case goes on, the spots will be found on the chest and upper extremities, and ultimately will appear on the lower part of the trunk and lower extremities. The spots will gradually become darker, and eventually assume a purple color. After some time the cuticle will be seen elevated over an odd macula, or filled with a fluid of a purple color, in a short time the cuticle becomes detached, and the subjacent parts, including the true skin and cellular substance will be remarked to be sphaculated to a greater or less extent — as the case progresses, the dead part will be thrown off, leaving ulcers of a considerable depth, or rendering the patient miserable by the total annihilation of an important organ.

With respect to the diagnosis between purpura and the Iodine disease, it will be noted that in the former the maculae appear on the lower extremities first, and that the disease almost invariably occurs in those whose constitutions have been broken down by long sea voyages, or are suffering under some other disease — such as typhus fever, phthisis, anasarca, chlorosis, or some other debilitating malady. Again, there is no pyralism — no bullae — no disagreeable odor — no constitutional derangement — but the grand characteristic distinction consists in the eruption. In the Iodine diseases, like the exanthemata, it shows itself first on the face, while in purpura it appears on the legs.

Or he may have referred to the paper by Hyde that appeared in the *Archives of Dermatology* in October, 1879 and that described all the known cases of a bullous rash developing after the administration of iodides. Not many had been reported, but they all were much alike. This type of rash may develop even after very small doses of the drug have been taken. It usually appears on the face, neck and dorsal surface of the arms and hands, and as a vesicle that rapidly increases in size and may remain discrete or may coalesce with neighboring vesicles to form bullae. In two thirds of Hyde's cases there were cardiac or renal complications, so that he put the question that others have asked since and that has never been answered satisfactorily. Why should patients with heart or kidney disease be predisposed to develop such an unusual type of skin reaction to iodine?

As I remember the scene, Dr Osler gave the impression of recognizing at a glance an uncommon clinical picture and then went on to show how a good clinician under such circumstances at once begins searching for similar cases. He and Dr Pratt were soon interchanging a barrage of names and literary allusions that were far over the heads



**FIGURE 1** Bullous Eruption after Iodide Administration  
"Over the backs of the hands and forearms are curious semi-spherical nodules ranging from 3 to 17 mm in diameter. The average size is 7 mm. A few are situated in the upper half of the forearms and are symmetrical. Today most of them are infiltrated with blood, have a bright, shining appearance and in color are from light to dark purple. Some are still firm, the larger ones are soft and fluctuant. They were quite tender at the start." (East Medical Records note by Dr Joseph H Pratt)

carditis, in which I, at least, assumed he might be interested. Instead, he began to talk about the rarer skin lesions that may develop following the use of iodides.

I wish that I could remember exactly what he said and how he said it. I am sure that he paid us the compliment of pretending to assume — since we youngsters recently had been welcomed to the company of educated men at a Harvard Commencement — that we were as familiar with

of the rest of us And the upshot was that we proceeded to the Treadwell Library to see what we could find

In those days the Treadwell Library was an ideal working library — a lovely room overlooking down from the walls benignantly at any readers, with a large central table at which one could spread out material to one's heart's content, and with shelves around the room containing enough books and periodicals so that surely one could find all

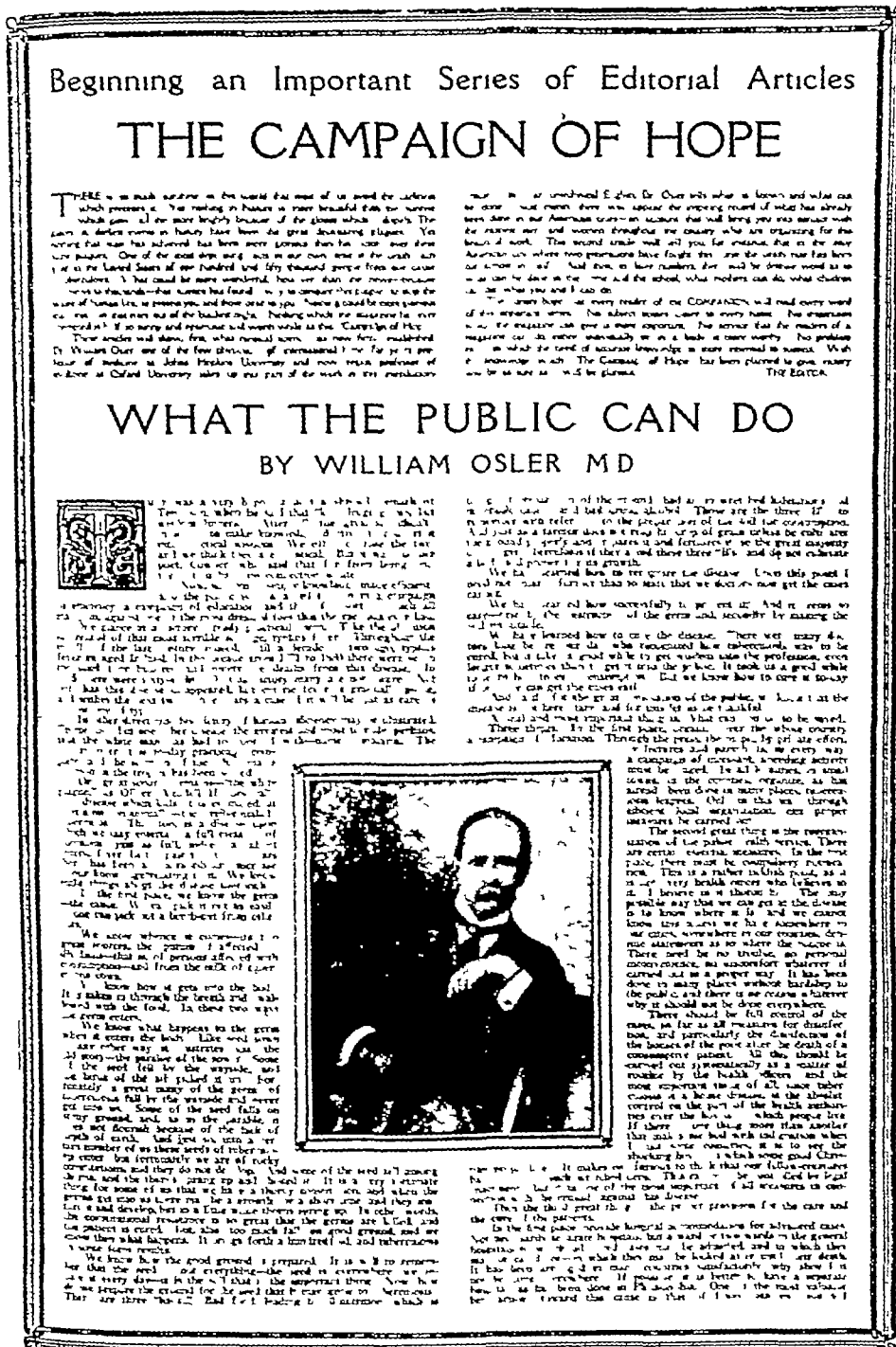


FIGURE 2 Title Page of Osler's Article in the February, 1910, Issue of *The Woman's Home* Companion (courtesy of the New York Public Library)

the hospital yard and in close proximity to the wards, with Stuart portraits at either end looking current literature pertinent to any subject that happened to be of immediate interest, and a good

many ancient books and periodicals that had accumulated with time. It was the pleasantest room in which to work that I have ever known.

Mrs. Myers presided over the library — always an awesome figure to the interns but an old friend of Dr. Osler's. On that morning, for once in our lives, we invaded her precincts with no hint of formality. Mrs. Myers and Dr. Osler greeted each other with distinct marks of affection, and then, as I recall it, Mrs. Myers got out for us to look at certain items dealing with bullous eruptions following the administration of iodide — perhaps Morrow's *Drug Eruptions*, which was first printed in 1887 and has for its colored frontispiece a bizarre example of iodism, or his article in the April and May, 1886 issues of the *Journal of Cutaneous and Venereal Diseases* on the same topic and reproducing the same drawing, or the more recent paper by Gottheil that had appeared in the *Journal of the American Medical Association* a few months previously. We could not find Hare's paper in the 1886 volume of the *New York Medical Record*, which described dynamic dilatation of the aorta, Dr. Osler mentioned this in connection, I presume, with our patient's endocarditis and anemia.

I cannot remember how long Dr. Osler's visit lasted. My recollection is that it was altogether too short and that it ended with a ceremonious parade to the Out Patient Department, headed by Dr. Pratt with Dr. Osler on his right, followed by Dr. Brigham and myself holding ourselves proudly erect, and ending with Dr. Parker, who ran ahead at every possible opportunity to open doors so that his seniors might encounter no physical inconvenience on their march.

Dr. Pratt tells me that a queer postscript should be added to this account of Dr. Osler's visit. Having deposited Dr. Osler and Dr. Pratt in a cab, the East Medical Service resumed its ordinary occupations. Dr. Osler wanted to go to the South Station, and Dr. Pratt accompanied him. Dr. Osler, apparently, disliked to hurry for trains, and so they got to the depot in ample time. They sat together in the stuffiness of a car that had been baked in the trainyard, and so they felt as though they were in a Turkish bath. Dr. Pratt asked Dr. Osler if he knew that one of his papers had been published in the *Woman's Home Companion*.

Dr. Osler replied that he had no knowledge of it. Dr. Pratt countered by citing the exact reference. And then Dr. Osler laughed and said, "That explains a great deal!"

A year before, Mr. Bok, editor of the *Ladies' Home Journal*, had asked Dr. Osler to write for the magazine a series of three articles on the American woman that would interest lay readers. Osler had given the matter considerable thought but finally refused, thinking that to do so was a little beneath the dignity of a Regius Professor of Medicine. However, in 1907 at a meeting in Ireland organized by the Countess of Aberdeen he had delivered a lecture, and this later was incorporated as an article in a booklet entitled *Ireland's Crusade Against Tuberculosis*, which had been privately published without copyright. Apparently an ingenious agent in this country had seen this article by Dr. Osler; had realized that he might use it without offending the law, had posed as Dr. Osler's American representative and had submitted it to the *Woman's Home Companion* as an original contribution. Dr. Osler told Dr. Pratt that until then he had never understood the letter of warm expostulation that he had recently received from Mr. Bok.

It is interesting how vividly Dr. Osler and his personality always impressed people who came in contact with him. To those of us who saw him that morning at the Massachusetts General Hospital thirty-five years ago, his visit seems like yesterday, and each recalls something different from it. Dr. Pratt remembers the episode at the South Station, Mrs. Myers still smiles over the memory of the surprised group of house officers as they learned that she and Dr. Osler were old friends, Dr. Brigham remembers his charm, Dr. Parker remembers his demonstration of palpatory percussion in the recognition of hydrothorax, and I subscribe to an interest in medical history that has grown through his influence.

This, I suppose, is the essential secret of successful clinical teaching — so to endow one's associates that each acquires some personal gift in the way of knowledge or approach to clinical problems that is not usual and settled but is inventive and, by adding new rhyme and reason to what was routine, is enduring.

319 Longwood Avenue

# MULTIPLE PERITONEAL AUTOTRANSPLANTATION OF SPLENIC TISSUE FOLLOWING TRAUMATIC RUPTURE OF THE SPLEEN\*

## Report of a Case in an Adult

RICHEY L. WAUGH, M.D.

BOSTON

THE purpose of this paper is to discuss multiple peritoneal autotransplantation of splenic tissue following traumatic rupture of the spleen and to present a summary of reported cases, together with the first report of a case occurring in an adult.

In the cases hitherto reported, all patients had in youth survived traumatic rupture of the spleen and later, either at reoperation or autopsy, numerous spleenlike nodules were found scattered over the various peritoneal surfaces, including the omentum, small and large intestine, diaphragm and pelvic cavity. Buchbinder and Lipkoff<sup>1</sup> consider the condition a clinical entity and suggest the use of the term "splenosis" to describe it. Despite the similarity, these spleenlike nodules should not be confused with accessory spleens or spleniculi, which are among the congenital anomalies most frequently found at autopsy.

It is apparent from a review of the literature that peritoneal autotransplantation of splenic tissue following traumatic rupture of the spleen is a rare condition. I have been able to find reports of only 15 cases, of which 9 are in the foreign literature and 6 in the American literature. An explanation for the small number of cases thus far reported is given by Hamrick and Bush.<sup>2</sup> These authors refer to the huge over-all mortality rate of between 90 and 100 per cent for traumatic rupture of the spleen and state that survivals are therefore relatively few in number. Consequently, the chances that such patients will come to abdominal surgical exploration or post-mortem examination are not very great. On the other hand, the actual occurrence of these splenic nodules in patients who have survived traumatic rupture of the spleen may be greater than has been reported.

The first known reference to the condition was that made by von Kuttner<sup>3</sup> in 1910. He found multiple splenic nodules at autopsy in a patient four years after splenectomy following rupture of the spleen due to a gunshot wound of the abdomen. He, however, regarded these nodules as accessory spleens and not as implants of splenic tissue.

Faltn<sup>4</sup> in 1911 was apparently the first to suggest that these splenic nodules were actually splenic implants. His patient was a nine-year-old boy who at the age of three had a ruptured spleen removed following an accident. During the next six years, he suffered with recurrent attacks of ab-

dominal pain, and an operation for chronic appendicitis was performed. At operation, multiple splenic nodules were found scattered throughout the abdominal cavity. One of these was removed, and on microscopic examination it showed the typical structure of spleen, including lymph follicles.

Von Stubenrauch<sup>5</sup> in 1912 reported similar multiple nodules, ranging from the size of hemp seed to that of a pea and with the color of the spleen. These were found on the greater omentum, transverse mesocolon and small intestine in a patient operated on for ileus who ten months previously had received a splenectomy for traumatic rupture of the spleen. Von Stubenrauch concluded that the nodules were a result of so-called "seeding" by splenic pulp, which was scattered throughout the peritoneum at the time of the rupture of the spleen.

In the case reported by Lee<sup>6</sup> in 1923, it was not stated whether the nodules were accessory spleens or implants. Von Küpperman<sup>7</sup> in his report in 1926 called the nodules accessory spleens. Shaw and Shafi<sup>8</sup> in their report in 1937 stated their belief that the nodules were true implants and not accessory spleens.

The 6 cases reported in the American literature include 2 cases reported by Jarcho and Andersen<sup>9</sup> in 1939 and single cases reported by Buchbinder and Lipkoff<sup>1</sup> in 1939, Hamrick and Bush<sup>2</sup> in 1942, Krueger and Mast<sup>10</sup> in 1942 and Boggs<sup>11</sup> in 1945. These reports contain excellent reviews or descriptions of this clinical entity and are well worth reading.

Buchbinder and Lipkoff<sup>1</sup> state that it has been shown experimentally that splenic tissue may be implanted in the peritoneum and readily survives transplantation. Von Stubenrauch<sup>12</sup> removed the spleen in several dogs and seeded the crushed splenic pulp throughout the peritoneal cavities. On sacrificing the dogs one to three months later, he was able to demonstrate the same picture that he had described in man. Marine and Manley<sup>13</sup> in 1920 and Perla<sup>14</sup> in 1936 showed the readiness with which autoplasmic splenic transplants grow in rabbits and albino rats, although these transplants were in the abdominal wall and not in the peritoneum.

Hamrick and Bush<sup>2</sup> state that Kreuter<sup>15</sup> in 1920 experimentally excised the spleen in monkeys and smeared the splenic pulp over the peritoneum. Several weeks or months later the animals were sacrificed and splenic nodules were found widely dispersed over the peritoneal cavity. Jarcho and

\*From the Surgical Service, United States Marine Hospital.

†Medical director, United States Public Health Service, chief of the Surgical Service, United States Marine Hospital.

Andersen<sup>9</sup> reviewed the literature and found cases of dogs that had had severe abdominal trauma, post-mortem examination revealing nodular implants of splenic tissue scattered throughout the abdominal cavities. These authors also stated that Griffin and Tizzoni<sup>16</sup> as early as 1883 had noted that partial splenectomy in dogs was followed by the development of spleenlike nodules in the peritoneum.

In this connection, Boyd<sup>17</sup> states that in some invertebrates the splenic tissue does not form a definite organ but is scattered beneath the serous coat of the gastrointestinal tract. He also states that some of the higher fishes exhibit splenic tissue divided into separate nodules. Clark<sup>18</sup> states that in fishes, turtles and frogs the spleen exists as an elongated body developed in the mesentery parallel and in close proximity to the digestive tube along the upper, middle or lower part of the intestine.

It therefore appears that the autotransplantation of splenic tissue is comparable to the not infrequent finding of multiple accessory spleens or spleniculi. Moreover, it is apparent that both these conditions represent a reversion to the primitive or atavistic state, in which splenic tissue does not form a definite organ but is strewn throughout the subserous coat of the gastrointestinal tract.

According to the literature, autotransplantation of splenic tissue has been observed only in young patients who have suffered traumatic rupture of the normal spleen. Hamrick and Bush<sup>2</sup> believe that the likelihood of success in grafting cells from splenic pulp on peritoneal surfaces is proportionate to the youthfulness of the normal spleen. These authors state that splenic-pulp cells of young persons probably have properties of increased viability or virulence much greater than those of similar cells in older persons.

The spreading or seeding of splenic-pulp cells on peritoneal surfaces is accomplished through the medium of the free blood present in the abdominal cavity following splenic rupture. After implantation, the nests of cells grow, and the nodules finally become encapsulated by fibrous tissue. On maturity, these splenic implants are found to have histologic structures not unlike that of normal spleen.

According to Hamrick and Bush,<sup>2</sup> parenchymatous cells of no other abdominal organ exhibit similar characteristics except possibly those of the uterine endometrium. The surgeon should keep this in mind and be able to differentiate splenic implants and endometriomas.

No cases have been reported of autoplasmic transplantation of splenic tissue following splenectomy for pathologic conditions of the spleen. This is all the more interesting since it has been shown by Jarcho and Andersen<sup>9</sup> that the number of these patients who survive and later come to reoperation or autopsy is much greater than that of patients

who survive splenectomy for traumatic rupture of the spleen.

Splenectomy for pathologic conditions of the spleen is usually accomplished without the spreading of splenic pulp over the peritoneal surfaces, but even if under unusual conditions such spreading occurred, the abnormal or diseased condition of splenic-pulp cells would probably hinder successful implantation. This view is also entertained by Shaw and Shafi,<sup>8</sup> who state that the removal of diseased spleens is rarely if ever followed by implants, in spite of occasional tearing with some associated hemorrhage during the excision of a particularly large viscus.

Of the 15 cases reported as showing autoplasmic transplantation of splenic tissue, there are only 9 in which the age of the patient at the time of occurrence of the rupture of the spleen is stated (Table 1). The recorded ages ranged from three to fourteen years, with an average of ten years. In striking contrast is a patient who was thirty-two years of age at the time of the rupture of the spleen and splenectomy. A report of the case follows.

A M R., a 37-year-old housewife, was admitted on March 14, 1944, for treatment of menorrhagia and metrorrhagia of 5 months' duration. She had an abdominal operation at the age of 28, at which time the appendix and right ovary were removed. At 32 she suffered an abdominal injury in an automobile accident. Immediately after the injury she was taken to a hospital, and 1 hour after admission a splenectomy for traumatic rupture of the spleen was performed. The postoperative course was apparently uneventful.

Three months before the present admission, a cervical polyp was removed on account of menorrhagia and metrorrhagia. This operation, however, gave only temporary relief from bleeding, and the patient noticed an increasing amount of low-abdominal discomfort, fullness and pain. She had had three children, each full term at the time of delivery. The last pregnancy had occurred 12 years previously. Physical examination revealed a well developed but obese woman who did not appear acutely ill. The skin and mucous membranes of the lips were slightly pale. The temperature, pulse and respirations were normal. The blood pressure was 122/76. Except for the abdominal and pelvic (vaginal) findings, the examination was negative.

The abdomen was obese and flabby. There were two operative scars—one an oblique scar over the left upper quadrant, and the other a midline scar over the lower abdomen. There was moderate tenderness to palpation in both lower quadrants and a questionable mass in the suprapubic region slightly to the left of the midline. Vaginal examination revealed a cervix with a transverse laceration and a moderate degree of ectropion. There was also a moderate amount of erosion of the cervix, with an area of blanching, apparently at the site of the attachment of the previously removed cervical polyp. The body of the uterus was anterior in position and slightly enlarged. There were no masses or tenderness in the right fornix, but in the left fornix there was a slightly tender and movable mass about the size of a hen's egg. This mass was thought to be either a pedunculated uterine fibroid or an ovarian cyst.

The urine gave a + test for albumin but was otherwise normal. The blood examination revealed a moderate hypochromic anemia, with a red-cell count of 3,400,000, a hemoglobin of 70 per cent and a hematocrit of 34 per cent. The white-cell count was 6400, with 47 per cent lymphocytes, 52 per cent neutrophils and 1 per cent large mononuclears. The sedimentation rate was normal. Blood Kahn and Hinton tests were negative.

Under pontocaine spinal anesthesia, the abdomen was opened through a low midline incision. There were many peritoneal adhesions involving the peritoneum of the anterior abdominal wall, the body of the uterus, the left ad



the sigmoid colon. The uterus was slightly irregular in contour and two or three times normal size. Both tubes and the right ovary were absent. The left ovary was cystic and three times normal size. Scattered over the serous surfaces of several loops of small bowel and the cecum were many small, reddish nodules varying in size from a pinhead to a small pea. The total number of nodules visualized in the limited abdominal wound exposure was about ten. These nodules were believed to be lymphoid tissue due to implantation of splenic pulp at the time of the previous rupture of the spleen and splenectomy. Further exploration of the abdomen by palpation revealed several stones in a flabby

healed by primary intention, and no vaginal discharge was present on pelvic examination a few days prior to discharge on the 20th postoperative day. The patient was advised to return later for cholecystectomy, but up to August 10, 1945 had not done so.

The pathological report, by Dr T F Crahan, was as follows:

Grossly, there are two small encapsulated tumor masses closely apposed to each other, the larger measuring 2.5 mm and the smaller 2 mm in diameter (Figs 1 and 2). On cut section the tumor masses have a slightly reddish color and

TABLE 1 Summary of Reported Cases

SOURCE	AUTOPLASTIC PERITONEAL TRANSPLANTATION OF SPLENIC TISSUE						
	DATE	HISTORY OF TRAUMA	AGE AT TIME OF DIAGNOSIS	AGE AT TIME OF RUPTURE AND SPLENECTOMY	REASON FOR EXAMINATION	LOCATION OF NODULES	NUMBER OF NODULES
Albrecht <sup>19</sup>	1896	Unknown	25	Unknown	Autopsy	Greater omentum, rectovesical pouch and both domes of diaphragm	Numerous
Schilling <sup>20</sup>	1907	Unknown	47	Unknown	Autopsy	Greater omentum, peritoneum of anterior abdominal wall and pelvis	42 on great omentum (several more elsewhere)
von Küttner <sup>3</sup>	1910	Yes	Unknown	Unknown	Autopsy	Scattered throughout the peritoneum	50-100
Faltn <sup>4</sup>	1911	Yes	9		Operation for chronic appendicitis	On loops of large and small intestines	Numerous
von Stubeusach <sup>5</sup>	1912	Yes	Unknown	Unknown	Operation for ileus	Greater omentum, transverse mesocolon and small intestine	Numerous
Oitmanns <sup>1</sup>	1919	Yes	Unknown	Unknown	Unknown	Throughout peritoneal cavity	Multiple
Lee <sup>6</sup>	1923	Yes	29	14	Operation for ileus	Small intestine and mesentery	Numerous (200-300)
von Kuppermann <sup>7</sup>	1936	Yes	15	14	Operation for postoperative hernia	Small and large intestines	100
Shaw and Shaff <sup>8</sup>	1937	Yes	20	Unknown	Autopsy	Abdominal wall, pleural cavity, liver, diaphragm, rectovesical pouch and great omentum	32
Jarcho and Andersen <sup>9</sup>	1939	Yes	8	6	Autopsy	Left dome of diaphragm, liver, stomach, lesser omentum, transverse colon, right kidney, rectum and bladder	Several dozen
	1939	Yes	20	13	Autopsy	Peritoneum, greater omentum, diaphragm and greater curvature of stomach	30
Buchbinder and Lipkoff <sup>1</sup>	1939	Yes	33	3	Operation for pelvic disease	Parietal peritoneum, great omentum, ileum, sigmoid and ascending colon	Numerous
Hamrick and Bush <sup>2</sup>	1940	Yes	13	9	Autopsy	Parietal peritoneum, pelvic cavity, omentum, serosa of large and small intestines and diaphragm	Approximately 75
Krueger and Mast <sup>10</sup>	1942	Yes	10	11	Laparotomy for adhesions	Both surfaces of omentum	20 or 30
Boggs <sup>11</sup>	1945	Yes	14	11	Operation for acute appendicitis	Small intestine	Several
Author	1945	Yes	37	32	Hysterectomy for fibroids	Small intestine and cecum	10 (visualized)

gall bladder and a mass of adhesions in the region of the splenic flexure of the colon.

The adhesions of the anterior abdominal wall, omentum, bowel and uterus were separated. A total hysterectomy was done, but the cystic left ovary, the larger cystic portions of which broke during the operative procedure, was not removed. Two small nodules were removed from the serous surface of the small intestine for pathological examination. Chromic catgut was used for ligatures and sutures, and plain catgut for the peritonealization of the pelvic cavity. Three grams of sulfanilamide was sprinkled in the pelvic cavity, and the abdomen was closed in layers with chromic catgut and Kaldernic sutures.

The postoperative course was uneventful, and the temperature the 5th postoperative day. The wound

are soft in consistence and the larger one shows several small, white follicles measuring less than 1 mm in diameter. Microscopically, the two masses consist of small portions of splenic tissue completely surrounded by a fairly thick, dense fibrous capsule. Where they are apposed the fibrous capsule fuses. The larger mass shows malpighian corpuscles which have prominent arterioles. One of the follicles has a germinal center, with prominent hyperplasia of the reticulum cells. The pulp is extremely cellular, but in some areas definite sinusoids can be made out. Most of the sinusoids are empty, but some contain red blood cells. There is prominent hyperplasia of the sinus endothelial cells and pulp reticulum cells. There are scattered eosinophils and occasional groups of plasma cells. The capsule is focally infiltrated with lymphocytes and

plasma cells, chiefly perivascular. These vessels are mostly thin-walled capillaries. A definite hilus cannot be seen, but in the smaller of the two masses there is a small capil-

report of peritoneal autotransplantation of splenic tissue occurring in an adult following rupture of the spleen and splenectomy



FIGURE 1 Photomicrograph of a Full Section of the Two Apposed Splenic Transplants ( $\times 20$ )  
Note the capsule, malpighian corpuscles and pulp

lary that seems to communicate with the pulp. The histopathological diagnosis is autoplasmic transplantation of splenic tissue.

This case is of unusual interest since the patient was thirty-two years of age at the time of the sple-

#### SUMMARY

The literature relative to peritoneal autotransplantation of splenic tissue following traumatic rupture of the spleen is reviewed briefly and discussed. Only 15 cases are reported in the literature. Of these, 9 cases are in the foreign literature and 6 cases in the American literature.

An additional case of autotransplantation of splenic tissue is reported and discussed. Its chief interest lies in the fact that the patient was thirty-two years old when splenic rupture occurred and splenectomy was performed.

These peritoneal splenic implants or nodules should not be confused with accessory spleens or spleniculi, which constitute one of the congenital anomalies most frequently found at autopsy, nor should they be confused with endometriomas.

The widespread location of these splenic implants or nodules bears a resemblance to the normal finding in some invertebrates, as well as in some of the higher fishes, in which splenic tissue does not



FIGURE 2 Photomicrograph of the Same Section at a Higher Magnification ( $\times 75$ )  
This shows two malpighian corpuscles, with lymphoid nodules and small arterial branches. Well formed trabeculae are not seen.

nectomy whereas in the previously reported cases the patients were children, the two oldest both being fourteen years of age. This is therefore the first

form a definite organ but is scattered beneath the serous coat of the gastrointestinal tract. This analogy therefore suggests that the condition can

be considered a reversion to the primitive or atavistic state

I am indebted to Passed Assistant Surgeon K M Endicott, Department of Pathology, National Institute of Health, United States Public Health Service, for his courtesy in making the microphotographs

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## GRANULOMA INGUINALE: A PROCTOLOGIC CONSIDERATION\*

JOSEPH BERKOWITZ, M.D.†

BOSTON

GRANULOMA inguinale was first described as a clinical entity by Conyers and Daniels in 1896, although the etiologic factor was not discovered until 1905 by Donovan at the Madras General Hospital in India. This disease has been considered a venereal one owing to the fact that the lesion is found in most cases on the genitals or scrotum or in the inguinal region, and also because of its frequent association in the same patient with syphilis, chancroid or lymphogranuloma.

The principal pathologic manifestation is found in the skin. The lesion begins as a small papule or macule, which enlarges, ulcerates and spreads by contiguity. The ulceration is covered with pink raised granulations that bleed easily on trauma. Progress of the disease is slow. Over a period of months or years the skin becomes granulomatous and indurated. During this time the patient is ambulatory and in apparently good health, with no evidence of systemic reaction. The pathologic lesion is a chronic inflammatory granuloma characterized by a specific diagnostic cell, a large mononuclear, in the cytoplasm of which are numerous round or rod-like structures known as "Donovan bodies." The preponderance of opinion concerning the nature of these bodies favors the belief that they are gram-negative, nonmotile bacilli in a state of encapsulation.

The incidence of granuloma inguinale is highest in the Negro race and in warm climates. Direct smears from an ulceration or a biopsy specimen from a granulomatous mass are invaluable in the diagnosis. Pathologic entities that present a similar clinical picture and must therefore be ruled out are syphilis, chancroid, tuberculosis, lymphogranuloma and cancer. Specific diagnostic skin tests and laboratory procedures for excluding these diseases are readily available. A specific skin test for the diagnosis of granuloma inguinale has recently been elaborated, but this method has not yet been made generally available. Numerous forms of therapy have been employed, such as x-ray, fulguration and surgical excision, but the best results have been obtained with antimony preparations given intramuscularly.

**CASE 1.** A 26-year-old Negro soldier was admitted to the Surgical Service of this hospital on September 25, 1944, complaining of perianal pain. For 3 months prior to admission he had had pain on defecation, which lasted for 1 hour after completion of the movement. There was no anorectal bleeding, no anal discharge or protrusion, and no change in the size or character of the stool. For 1 week prior to admission there had been severe chafing about the anus, causing pain on walking and soreness on sitting. In 1935 the patient had had gonorrhea, which was treated. There was no history of a penile lesion or of injections for syphilis.

Physical examination disclosed a well-developed Negro walking in obvious pain. On both sides of the anus and directly opposed so as to make contact there were two areas of ulceration, each measuring 1.5 by 1.5 cm. The surfaces of these ulcerations were covered with raised red granulations. The underlying tissue felt nodular and indurated. There was no evidence of fissure, abscess or fistula. The sphincter tone was increased, and digital examination caused severe pain.

\*From the Surgical Service, Lovell General Hospital, Fort Devens, Massachusetts.

†Junior assistant surgeon, Rectal Clinic, Boston Dispensary; assistant in rectal diseases, Brockton Hospital; formerly, surgeon in charge of rectal diseases, Lovell General Hospital, Fort Devens, Massachusetts.

The remainder of the examination was temporarily deferred, and it was suspected that the patient had an anal fissure.

Routine laboratory studies on admission were within normal limits. A Kahn test was negative. A routine Frei test was positive at 72 hours. The soldier was given hot sitz baths, with symptomatic relief. Further examination several days after admission was entirely within normal limits except for the indurated ulcerations. Sigmoidoscopy revealed no disease in the rectum or lower sigmoid. There was no evidence of anal fissure.

The ulcerations did not heal under palliative treatment, and the underlying induration persisted. On October 6, operation was performed. Minute abscess cavities were found beneath the ulcerations. On the left side of the anus these connected with each other and with a deep crypt at "9 o'clock" on the anorectal line. Fistulotomy was performed, with adequate shelving of the skin edges. The abscess cavities did not connect with the anal canal on the right side. These cavities were unroofed and packed with iodoform gauze. Sections of tissue were sent to the laboratory. Post-operative treatment consisted of hot sitz baths three times daily, a regular diet and mineral oil by mouth. Healing was slow.

The pathological report stated, in part, that the sub-epithelial layer was occupied by a large number of clear cells with vacuolated cytoplasm and small dark-staining nuclei (Fig 1). Some of these cells contained coccoid or rodlike Donovan bodies. The diagnosis was granuloma inguinale.

The patient was placed on intramuscular Fuadin\* therapy, receiving 1.5 cc on the 1st day, 3.5 cc on the 2nd day, 5.0 cc on the 3rd day and 5.0 cc every third day for six doses —



FIGURE 1 Case 1

Photomicrograph of the biopsy specimen shows marked hyperplasia of the epithelium. Characteristic large clear cells occupy the papillae and upper layers of the corium. Occasionally these cells contain Donovan bodies.

a total of 40 cc. There was no reaction to the drug, and no pain resulted from the injections. The operative wounds closed steadily, leaving a soft healed scar with loss of normal skin pigment. Three weeks after the beginning of Fuadin therapy, the wounds were healed, and the patient was returned to duty.

In the above case the patient was suspected of having an anal fissure because of the typical history of severe pain associated with bowel movements.

\*Sodium antimony-III bisacatechol disulphonate of sodium manufactured by the Winthrop Chemical Company, New York City.

and lasting for one hour following them. The two areas of ulceration were thought to be due to chafing arising from intensive military training. They were discrete and directly apposed and were covered with pink granulations such as are found in all healing wounds. The positive Frei test was significant in that it indicated the coexistence of lymphogranuloma inguinale. It would have been impossible to make the correct diagnosis from the appearance of the lesion alone, and except for the pathological report it would have been entirely missed. Had the diagnosis been suspected, it might have been confirmed sooner by smear or by biopsy.

**CASE 2** A 24-year-old Negro soldier was admitted to the Surgical Service of this hospital on October 25, 1944, complaining of anal pain and purulent anal discharge. In 1934, he first noticed a small papule on the right side of the anus. This papule caused no discomfort but slowly increased in size until it was as large as a walnut. In 1942, an abscess developed at the site of the mass, and this was followed by a fistula. Some type of surgery was performed at a civilian hospital, but apparently the growth was left undisturbed. The patient felt well until May, 1944, at which time a right perianal abscess recurred. This was incised and drained. Drainage ceased for a short period but recurred in the following September, when the patient was admitted to an Army hospital and transferred to the Lovell General Hospital for further treatment and disposition. He denied having had gonorrhea but stated that he was taking "injections for his blood."

Physical examination disclosed a well-developed Negro in no distress. There was a large granulomatous mass measuring 5 by 3 cm just to the right of the anus. It extended medially to involve the anal canal and terminated laterally in two long, well-healed but indurated scars (Fig 2). The center of the

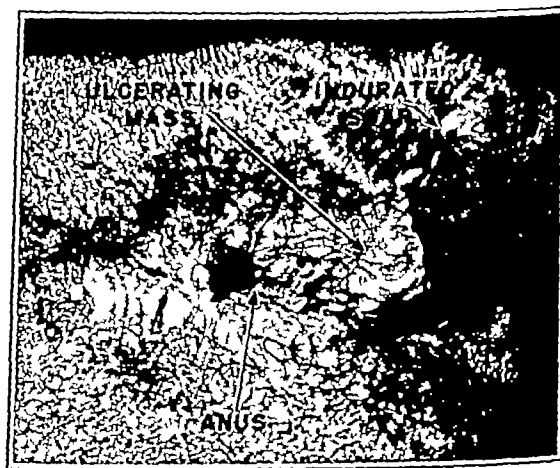


FIGURE 2 Case 2

Photograph of the granulomatous mass of ten years' duration.

mass was ulcerated and covered with a purulent secretion, beneath which were easily bleeding pink granulations. Digital examination was negative except for hard indurated tissue of the right anal wall. The sphincter tone was slightly diminished. There were slight internal hemorrhoids.

Routine laboratory studies were within normal limits. A Kahn test was negative. Consultation was held with the Venereal Disease Section, with a resultant diagnosis of early latent syphilis. A Frei test was negative at 72 hours. On October 26, a biopsy specimen was taken under local anesthesia.

The pathological diagnosis was chronic suppurative, non-specific inflammation. The degree of sphincter involvement could not be determined, but it was considered certain that extensive surgery would be required to eradicate the lesion.

The patient was returned to his unit on November 13 with a diagnosis of nonspecific granuloma, and it was requested that he be separated from the Service.

On December 14, a report was received from the Army Medical Museum on the biopsy material submitted to it, the diagnosis was *granuloma inguinale*. The patient was recalled at once to the hospital. He was complaining of a foul-smelling, purulent anal discharge. A biopsy was repeated. The resultant pathological report stated that here and there just beneath the epithelium there were marked edematous patches and a few large cells, with clear cytoplasm and round nuclei, some of which contained masses of rodlike or coccoid Donovan bodies deeply stained with blue (Fig 3). The diagnosis was *granuloma inguinale*.

Intramuscular Fuadin therapy was instituted as in Case 1. After conclusion of the course, the patient was allowed a rest

owing to the tendency to recurrence. Intramuscular Fuadin salvaged for military service a soldier who might otherwise have been lost to it.

### SUMMARY

*Granuloma inguinale* is a chronic, progressive skin infection of the genitals, scrotum and inguinal regions. It occurs infrequently about the anus. Its

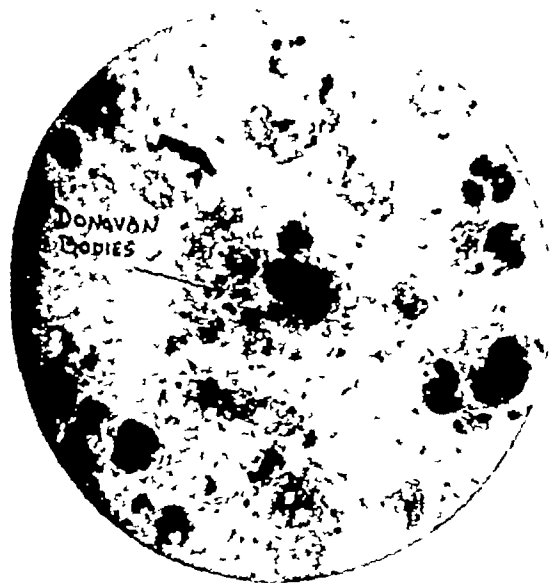


FIGURE 3 Case 2

This photomicrograph of a stained smear shows numerous intracellular oval (Donovan) bodies in the cytoplasm of a large macrophage.

of 1 week. There was no reaction to the drug. On December 16, the patient stated that he was having much less drainage. The lesion appeared unchanged, but within the following week the granuloma decreased considerably in size and showed much less surrounding induration. Drainage had practically ceased, and there were no complaints. On January 15, 1945, a second course of Fuadin was begun. It was completed on January 24, and the patient was returned to duty. Subsequently the granuloma disappeared entirely, leaving a small area of skin in which the normal black pigment was absent (Fig 4).

In this case *granuloma inguinale* had been present for approximately ten years, and the advanced granulomatous stage of the disease was well represented. Even though the diagnosis was suspected on admission, it was missed because of a poor section of tissue taken for biopsy. Two courses of Fuadin were given, a procedure that is recommended

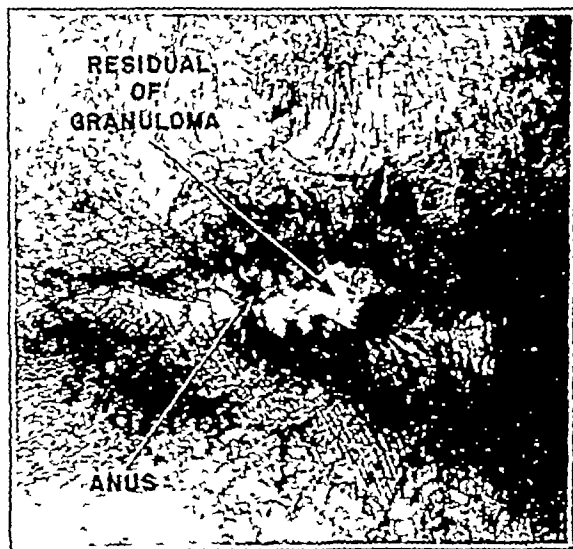


FIGURE 4 Case 2

Photograph showing the healed lesion after two courses of Fuadin.

etiologic agent is a gram-negative, nonmotile bacillus identifiable by smear or biopsy in the state of encapsulation as a "Donovan body." The disease occurs primarily in Negroes.

Two cases are presented involving the region about the anus, one in an early ulcerating stage and the other in an advanced granulomatous stage. The response to Fuadin was excellent in both cases but was especially dramatic in the second case, in which there was a lesion of ten years' duration.

475 Commonwealth Avenue

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## MEDICAL PROGRESS

### RESEARCH IN PHYSICAL MEDICINE (Concluded)

ARTHUR L. WATKINS, M.D.\*

BOSTON

#### ELECTROTHERAPY

##### *Diathermy*

Medical diathermy has been defined as the therapeutic use of heat generated in body tissues by a high-frequency current that has insufficient local intensity to produce temperatures high enough to destroy or injure tissues. These currents are applied locally by three methods: conventional long-wave diathermy with contact metal electrodes, short-wave diathermy with an electric field, air space or insulated electrodes being used, and short-wave diathermy with an electromagnetic field, a cable or coil being employed. Conventional or long-wave diathermy frequency is between 500,000 and 3,000,000 cycles per second, whereas short-wave diathermy frequencies are between 10,000,000 and 100,000,000 cycles. At the present time short-wave diathermy is used much more extensively than is long-wave diathermy, because of its ease of application, the somewhat less danger of burns and the more uniform temperature effects. The fundamental laws and concepts of alternating current phenomena on which short-wave diathermy technic is based have been well described in Osborne and Holmquest's<sup>36</sup> textbook on electrotherapy. A shorter summary has recently been written by Holmquest.<sup>37</sup> In summary, he states that in practice there are two methods of applying high-frequency power to tissue for treatment purposes — by means of the high-frequency field such as exists between plate electrodes, with or without an air space between electrodes and skin, and by means of the high-frequency magnetic field that is set up by the high-frequency current flowing through a coil, which is wound around the part to be treated or wound into a circular pad and placed over the tissues in which it is desired to generate heat.

Much investigative work has been done to determine the heating characteristics of these two methods. It has been shown that, with the high-frequency electric field, heating depends on the specific conductivity of the electrolyte exposed to the field and rises to a maximum for a certain conductivity. As the frequency of the field is increased, the conductivity at which maximal heating occurs also increases. It has been shown that there is a linear relation between frequency and specific con-

ductivity for maximal heating. With a frequency of 10 megacycles (wave lengths of 30 meters), maximal heating occurs in a sodium chloride solution having a specific conductivity of 5.4 for a concentration of 0.0045 gm.-mols per liter or 0.0263 gm per 100 cc of solution. Since for dilute solutions conductivity is proportional to concentration, one can readily determine the approximate concentration of sodium chloride solution into which the rate of heat production would be graded for various frequencies. The concentration of sodium chloride having the conductivity of blood plasma is 0.85 gm per 100 cc of solution. So that heat shall be produced predominantly in the vascular type of tissue where it is normally produced through energy metabolism, an extremely high frequency must be employed. It must not be inferred, however, that, the approximate specific conductivity of various organs of the body being known, frequencies can be selected to elevate the temperature of these organs without elevating the temperatures of other tissues and organs. Efficiency of the blood stream in dissipating heat and conveying it to other structures of the body tends to equalize temperatures and hence to prevent such specific heating.

Regarding the second method of applying high-frequency energy to the tissues, experiments have shown that the induction field generates heat in an electrolyte in direct proportion to the conductivity of the electrolyte. Such a field should produce heat dominantly in vascular tissue. Actual measurement of temperatures obtained in the deep tissues of living subjects has confirmed this theoretical deduction. From time to time claims are made for specific biologic and bactericidal effects of various frequencies. Careful investigators seem agreed, however, that the only demonstrable effects of short-wave diathermy are a production of heat and the physiologic responses that normally follow production of heat in tissue. Hence, the method of applying short-wave diathermy that develops heat primarily where oxidation produces it naturally in the human body, thereby inducing and maintaining active hyperemia and permitting the warmed circulating blood to convey heat to other tissues, seems to be the preferable manner of treatment of all conditions that might be benefited by such therapy.

The technic of application of short-wave diathermy has been well described in the standard textbooks

\*Associate in medicine, Harvard Medical School; chief of physical medicine, Massachusetts General Hospital.

Regulation of dosage, however, is still empirical. It is necessary to rely on a comfortable heat sensation of the patient's skin in measuring doses, since the milliammeter on the apparatus does not measure the energy passing through the patient. Some experimental work has been done on the measurement of field strength, but these methods have not as yet been applied clinically.<sup>38</sup> Until further evidence is forthcoming, it is sufficient to say that the physiologic effect of diathermy is simply that of production of heat in the tissues.

#### *Electrodiagnosis*

The chief diagnostic function of specialists in physical medicine is appraisal of excitability of nerve and muscle by stimulation with appropriate electrical current. In considering the methods used for this purpose, the average physician or surgeon has been cognizant only of the test for the so-called "reaction of degeneration," as described by Erb. Recent developments in electrical engineering have made available for experimental and clinical use new instruments capable of producing currents of easily measured strength, duration and frequency of impulse. A number of laboratory and clinical studies based on these new methods have been published in the last few years. They are of particular interest at this time because of the frequent occurrence of peripheral-nerve injuries among war casualties.

In Erb's test, faradic and galvanic currents are used, and the preservation of normal responses to these currents serves to distinguish severe peripheral-nerve injuries from minor lesions, upper-motor-neuron disease and hysterical paralysis. The limitations of this test are, however, frequently overlooked. Of first importance is the fact that changes in the electrical reactions of paralyzed muscles do not appear, even after complete severance of the motor-nerve supply, before a minimum of four to five days and may not be completely developed for two weeks. Electrical tests are therefore of no diagnostic value unless time is allowed for these changes to occur. The responses of muscles that when tested for a sufficient length of time after injury indicate loss of conduction of the normal nerve impulse and degeneration of intramuscular nerve fibers have been described by Erb as the reaction of degeneration. Recently Pollock et al.<sup>39</sup> reinvestigated Erb's conclusions, making use of modern apparatus, and found that his description was essentially accurate. Denervated muscles do fail to respond to a faradic current when stimulated percutaneously. This is not absolutely true, however, for even completely denervated muscles respond to the faradic current if a sufficiently high voltage is used. It should be further pointed out that although only the faradic currents were used by Erb for this test it is more usual at present to employ a 60-cycle alternating, sinusoidal current, since it

is of proper frequency to produce a tetanic contraction in normal muscle and the separate impulses are of sufficiently short duration so that the denervated muscle does not respond with the voltage of current usually applied clinically. Consequently, a more accurate description of such a reaction would be to say that there is loss of response to a tetanizing current.

The type of response to stimulation by direct or galvanic current is of equal or even greater importance. Normal muscles respond to a direct-current impulse by a single quick twitch and rapid relaxation. Denervated muscles, on the other hand, with the same type of stimulus show a slow, wave-like contraction, which is frequently sustained to a lesser degree without complete relaxation so long as the current is applied. Pollock et al. describe this response as a tetanic contraction and emphasize its importance in following the state of innervation of muscle during various stages of degeneration and regeneration. Doupe<sup>40</sup> studied this response of denervated muscle to direct-current stimulation by means of simultaneous mechanical and action-potential recordings. He found that the sustained contraction was explained by repetitive excitation and described the phenomenon as galvanotonous, which is perhaps a better description than Pollock's, since clinically the contraction is not so great as that of a complete tetanus. Doupe also found that the temperature of the denervated muscle was below normal and that the slowness of contraction could be partially explained on this basis, since the prolonged excitation factor was also accentuated by cold, as was a hyperirritability to currents of long duration and threshold strength.

In addition to the sluggishness of contraction on galvanic stimulation, Erb mentioned a change in the response to positive and negative currents. Whereas the cathode-closing contracture is normally greater than the anode-closing contracture, during denervation the responses may be equal or occasionally reversed. Pollock et al.<sup>39</sup> and other observers<sup>41</sup> have found that the threshold response to both cathode and anode stimuli may become equal during denervation but have never seen true reversal. Pollock has emphasized another feature of the degenerative reaction to direct-current stimulation — namely, hyperirritability. This may be more apparent than real, however, since the muscle contraction is increased because of prolonged excitation.

In addition to stimulating muscles directly with galvanic or tetanizing (faradic) current, it is also advisable to test conduction of nerve impulse by stimulating the nerve directly whenever possible, preferably above the site of the lesion. For this purpose either galvanic or faradic current may be used. The degenerated nerve does not transmit either current, and in this case responses are obtained only when the muscle is stimulated directly. Preservation of conduction along the nerve and of normal

faradic response when the testing is done sufficiently long after injury is accordingly of definite value in separating severe from minor injuries

These electrical tests described are, however, of little value in determining the first signs of recovery or of nerve regeneration, since it is generally accepted that voluntary return of function precedes return of faradic response. For accurate quantitative study of electrical excitability of nerves and muscles, the factors of current strength, duration and rate of increase of potential must be considered. Electrical generators are now available that enable one to control and measure stimulation. It has been found that when the development of current is essentially instantaneous, as with condenser discharges or square-wave impulses, there is a definite relation between the strength and the duration of impulse required to induce a barely perceptible standard or threshold contraction of the muscle. By stimulating muscles with currents of assorted strengths and durations, it is possible to plot the responses in the terms of a strength-duration curve that gives a graphic representation of the electrical excitability. Repeated determinations of such curves give fairly accurate qualitative measures of excitability, and at times changes may be detected in these curves that indicate beginning regeneration before it can be detected clinically.<sup>42, 43</sup> Such a change may be either a shift in the total curve toward normality or the presence of a break in the curve, indicating fibers of different excitability, owing to the arrival in the muscle of some regenerated nerve fibers.<sup>44</sup>

An arbitrary point on the strength-duration excitability curve has been designated as the *chronaxie*, or time factor of excitability. The first step in *chronaximetry* is to measure the voltage of current necessary to cause a liminal response when a unidirectional current of long duration is applied. This measurement is called the *rheobase*. The length of time that a current of twice the *rheobase* voltage must be applied to produce the same response is the *chronaxie*. Normally the *chronaxie* is extremely short, — 0.001 second or less, — but with denervation it becomes ten or even more than a hundred times greater. *Chronaxie* measurements are of greater quantitative value than are galvanic and faradic tests, but they do not offer so complete information as does determination of the whole strength-duration curve and are subject to more possibilities of error in the single determination as compared with the many points on the strength-duration curve.

Currents of various wave forms have also been employed to stimulate muscles for electrical diagnosis.<sup>45</sup> These may be in the shape of triangles, with a gradual increase of current to a peak and a similar decline, or progressive currents, or the wave form may be that of a true sine wave. The currents are used to measure another factor in

electrical excitability — namely, the power to accommodate to a slow change in potential. Because of this power, normal muscle does not respond to currents with a slow increase of potential except at high-current value. Denervated muscles, however, lose this characteristic and consequently respond to progressive currents of long duration and to extremely slow sinusoidal currents of low voltage. This change in accommodation, as indicated by the responses to progressive currents of long duration or to sinusoidal currents of low frequency, coincides with the changes in other measurements of excitability previously mentioned. Generators capable of producing progressive currents and low-frequency sine waves are to be found only in experimental laboratories, and consequently these tests do not have a wide clinical use.

All measurements of electrical excitability must be interpreted in proper relation to the time elapsed since injury or surgery. First, as previously mentioned, one or two weeks must elapse for the possible appearance of degeneration. Later, when one looks for regeneration, the maximum speed of recovery, approximately 4 millimeters a day, must be considered. Local factors, such as atrophy of the skin, edema and ischemia, may cause variations in the results. Perhaps most important of all is the skill, experience and diligence of the investigator in developing a standardized technic so that the results of one examination may be compared with those of another. The most valuable and accurate results are obtained by using a battery of electrodiagnostic tests, which are then repeated at stated intervals to determine the state of progress.

A new and entirely different method of electrodiagnosis, known as *electromyography*, makes use of the recording of small electrical potentials from muscles at rest or during voluntary contraction. Since these potentials are of extremely low voltage and short duration, a highly sensitive amplifier and recording system, such as the cathode-ray oscilloscope or amplifiers employed for recording brain potentials, must be employed. Bipolar electrodes are used, either percutaneously or by inserting a concentric needle into the muscle to be investigated. With these technics normal resting muscles give rise to no electrical discharges. During voluntary contraction, action potentials of a relatively high frequency and voltage and characteristic appearance are recorded.<sup>46</sup> These action potentials are, of course, not obtained in paralyzed muscles with complete denervation. Partially denervated muscles, on the other hand, may discharge scattered diphasic spikes, indicating some motor-unit activity, although no visible contraction is observable. The appearance of these spikes accordingly quickly differentiates a complete from a partial lesion.

In the case of complete degeneration, no action potentials are recordable, but if a proper type of amplifier is used, such as a cathode-ray oscillograph,



tiny spontaneous resting discharges of low voltage and duration may be recorded and identified as fibrillation of denervation, giving positive evidence of a complete lesion<sup>47</sup>

Even with this sensitive type of instrument, there is a necessary long period of waiting before the slow process of nerve regeneration can be detected peripherally in the muscle. Electromyography is, however, of considerable value in picking up the first signs of neurotization of muscle in the form of spontaneous discharges of high voltage, indicating beginning motor-unit activity.

Another electrical aid in the measurement of nerve function is determination of skin resistance. For this purpose Richter and Katz<sup>48</sup> have described a simple dermatometer suitable for quickly mapping areas of high resistance to the passage of a direct current. These areas correspond to the distribution of sensory innervation of peripheral nerves, particularly the ulnar and median. The obvious advantage of such a test is that it is completely objective and does not require the co-operation of the patient. It is especially useful in cases of suspected malingering or hysteria. In my experience, the regeneration of sensory nerves can be detected much earlier by the usual clinical test of sensation than by measurement of the skin resistance. In some cases there is a lag of several months after sensation has returned before the skin resistance decreases to normal values.

#### *Electrotherapy for Denervated Muscles*

The value of electrical stimulation of a denervated muscle has frequently been debated in the literature<sup>49-52</sup>. It is generally conceded, however, that stimulation of muscles during the first few weeks following denervation does not prevent the occurrence of denervation atrophy. The results in experiments that were continued for longer periods of time indicate that the rate of atrophy in the third and fourth weeks and later is considerably delayed by appropriate electrical stimulation of the denervated muscle<sup>53</sup>. It has also been shown that although the rate of regeneration of the nerve is not affected by this treatment the return of voluntary muscle contraction is enhanced by electrotherapy and that the degree of fibrosis is lessened according to histologic examination. In the light of more recent studies, the negative effects of galvanic stimulation of denervated muscle have been explained as due to ineffectual or too infrequent stimulation. Daily treatment has been found to be more efficient than treatment on alternate days, and for optimum effect a stimulus should be chosen that will produce a maximal tension during contraction<sup>54</sup>.

In view of the latest experimental work, it appears that the ordinary type of clinical muscle-stimulating apparatus is inadequate to achieve optimum therapeutic results. The rate of rise of

each impulse should be slow, and the frequency of impulses also should be slow, in the neighborhood of 10 to 25 per second, in order to cause maximum contraction of the denervated muscle with a minimum of current strength<sup>55</sup>.

Recent experiments have also shown that the dangers of fatiguing muscles have been overemphasized in the past. Marked fatigue through artificial stimulation or forced exercise was found to have no deleterious effect on regeneration. It now seems apparent that maximum results in strengthening a muscle can be obtained only by producing a maximal degree of tension<sup>54</sup>.

#### *Ion Transfer (Iontophoresis)*

Direct current may be used to drive certain medicinal electrolytes into tissues by the force of the polar reactions. The depth of penetration, however, is limited because of the far higher velocity and greater number of the tissue ions. The foreign ions introduced through the skin lose their electrical charge and are precipitated as soluble or insoluble compounds in the superficial tissues. The speed of circulation also serves to dilute the new ions quickly. In spite of these limitations, definite local and systemic effects can be produced by this method.

The drugs most widely used for the vasodilatory effect are histamine and mecholyl (acetyl-beta-methylcholine chloride). There are a great many clinical reports in the literature describing the use of these and other drugs in ion transfer. These have been summarized by Osborne<sup>56</sup>. Very little fundamental research has been done, however. More work like that of Pereyra<sup>57</sup> is needed to clarify the subject. He studied microscopically the penetration of copper by iontophoresis in experimental animals, and found that the greatest depth effects were obtained when a solution such as aerosol MA was added to inhibit the binding of copper by tissue proteins. Quantitative studies by Molitor and Fernandez<sup>58</sup> provide data for safe dosage.

#### HYDROTHERAPY

The use of water for therapeutic purposes is well established. Certain physical characteristics are recognized to be of importance. Water is an extremely flexible therapeutic agent, being easily changed from a liquid to a gaseous or solid state within relatively narrow temperature ranges, which may be easily measured. It is an excellent heating or cooling medium because of its high conductivity. Since it has a high specific heat, large amounts of heat are necessary to increase its temperature, and hence it is an excellent cooling agent. Similarly, it liberates a large amount of heat when cooled, making it a good heating agent. The latent heat of vaporization is high, and the heat lost in insensible perspiration is consequently significant in the regulation of the body temperature. The evaporation of sweat accounts for the ability to lose heat rapidly. The

buoyant effect of water during immersion is taken advantage of in forms of muscle re-education with underwater exercises

The mechanical impact of water is also known to produce physiologic responses. The type of impact may be varied, as with showers, douches, bubbles and so forth, and sedative and stimulative effects can be observed clinically. The exact mechanism of these reactions has never been extensively investigated and is a field of research in physical medicine that needs to be further developed. The best known effects of water are those that are dependent on its temperature, and these have been discussed previously.

### MECHANOTHERAPY

#### *Massage*

Knowledge of the physiologic effects of massage is rather limited. In actual practice, massage is usually preceded by application of heat and frequently followed by exercise. Improvement in circulation, relief of muscle spasm and an increase in joint range and strength of movement may be readily observed clinically. The exact role of massage in securing these effects has received little investigative study. Recent reviews on the physiology of massage<sup>59, 60</sup> refer to studies done for the most part twenty to twenty-five years ago. Papers published since then have been almost exclusively clinical in nature, with the emphasis on technic. The early studies suggested that the twenty-four-hour excretion of nitrogen was increased on days that massage was administered. Diuresis and an increase in oxygen consumption and carbon dioxide production following general or abdominal massage have also been observed. More recent workers have failed to find any significant alteration of the metabolism in the normal subject, and at the present time it is generally believed that whatever metabolism changes may be produced by massage are secondary to the mechanical influence on the circulation of the parts concerned.

The effects of massage on circulation are more definite and are easy to demonstrate. Light stroking has been shown to produce an almost instantaneous, although transient, dilatation of the capillary vessels, with a more enduring effect when the pressure is heavier.<sup>61</sup> Photographic studies of capillary circulation have also indicated changes in vessel walls that permit the passage of leukocytes. Some observers have found that the number of circulating red cells may also be increased by massage, although the exact mechanism is not explained.<sup>62</sup> It is well known that lymphatic circulation is increased by massage and passive motions<sup>63, 64</sup>

It is inferred by clinical observation that massage affects the nervous system. Part of the dilatation of blood vessels is thought to be effected through sympathetic reflexes. Massage is probably most frequently employed for relief of pain resulting from

muscle spasm. Massage is also used for its general sedative effect and for its hypnagogic action. Massage is also said to have stimulative effects on the neuromuscular apparatus. It is certainly an adequate stimulus for exciting tendon reflexes in spastic patients. There is, however, an absence of studies that explain the mechanism of such effects, which are thought to be achieved through the action of massage on the nerves and muscles.

The practice of massage at present seems to be more of an art than a science. Physicians and technicians through years of experience may learn how to achieve the desired results, often by an individual technic. Prescription of massage consequently amounts to instructing the technician in the results desired, whether stimulative or sedative, and including instruction in the type of manipulation to be avoided. Considering that this method of treatment has been observed clinically to produce important beneficial effects in a large variety of conditions, it is unfortunate that more scientific knowledge concerning the mechanisms of its actions is not available.

#### *Exercise*

The subject of exercise has many ramifications into the fields of mechanics, biochemistry and physiology in health and disease. Attention is called to several recent reviews. Elkins<sup>65</sup> has emphasized that those prescribing therapeutic exercise should have a knowledge of the basic principles involved in muscular action. One of the primary factors relates to the mechanics of movement. The bones and joints make up a fairly intricate lever system, with changing forces depending on the angle of pull. Two other physical properties of muscle of considerable significance are its elasticity and its extensibility. Contractility of muscle varies with its length, and this has to be taken into consideration in performing re-education exercises. The control of muscle movement through the nervous system includes resting and postural tonus, as well as co-ordination and skillful activity. These topics have been briefly reviewed by Elkins, who also cites further references.

An aspect of locomotion of considerable importance is that of posture or body mechanics. From the point of view of the physician, there is a strong feeling, based on clinical evidence, that good posture is essential for health and that poor body mechanics may be responsible for a number of pathologic conditions. This point of view has been stressed for a number of years by Goldthwait, Brown, Swaim and Kuhns<sup>66</sup> and was recently summarized by Hansson.<sup>67</sup> That stresses and strains on joints and supporting structures may result from poor mechanics is fairly obvious. Physiologic studies on the effects of posture on the various systems of the body, however, have not produced evidence in defense of the medical opinions of the relation be-

between posture and disease, except in some extreme cases, such as scoliosis with compression on the thorax Hellebrandt and Franseen<sup>68</sup> have shown that compensatory mechanisms are developed in man that cancel the apparent mechanical disadvantage of the vertical stance in overcoming gravitational stresses Standing has been found to be cheap in terms of metabolic cost, and it has yet to be unequivocally demonstrated that improvement in body mechanics is associated with a significant decrease in exchange of energy<sup>69</sup> The circulatory system is probably most affected by posture The blood pressure decreases with the erect position, but there are many compensatory mechanisms that act to overcome the disparity between the size of the vascular bed during standing and the volume of flow Involuntary postural sway may be of considerable importance in stimulating reflex activities of vital centers located in the medulla, making circulatory adaptation more efficient Further studies of these compensatory mechanisms in health and disease are necessary to put the concept of what is correct posture on firm scientific ground

Another aspect of exercise that has lately aroused considerable interest is the problem of general physical fitness Much of the recent work is subject to rules of military secrecy and has therefore not yet been published Physical fitness has frequently been assessed by exercise tests, such as the step test or treadmills and bicycle ergometers During such periods of exercise observations are made of the circulation and respiration and of various aspects of blood chemistry Over a hundred papers on this subject have recently been reviewed by Taylor<sup>70</sup> Physical training has been found to increase exercise performance The physiologic results of training indicate that except for a small but consistent reduction in heart rate, changes in resting functions are either nonexistent or slight In submaximal work, mechanical efficiency is increased by training and physicochemical blood factors depart less from their resting values Coincident with substantial training, increments in maximal work output, maximal blood lactate, oxygen consumption and oxygen depth undergo increase Improvement in athletic type-fitness tests amounts to as much as 20 per cent Absolute muscle power has been shown to rise 30 per cent with training but is indefinitely maintained in the post-training period, whereas endurance depreciates rapidly to 50 per cent<sup>71</sup>

The problem of fatigue has stimulated considerable investigative work, including study of mental and emotional variables Neurocirculatory asthenia, the so-called "effort syndrome," is generally believed to be a psychoneurotic manifestation The general problem of muscular exercise and fatigue in disease has been well reviewed by Simonson and Enzer<sup>72</sup> It is to be expected that the final analysis of the

large body of new information on exercise and fatigue that is being developed in relation to the recent war will place exercise therapy on a firm scientific basis

OCCUPATIONAL THERAPY

The medical profession in general is little acquainted with the potential value of occupational therapy Those clinically familiar with it have realized that muscular strength, co-ordination and adaptability of injured or diseased parts may be gained under the skilled direction of an occupational therapist It has been emphasized that mental as well as physical function is stimulated by such activities Psychiatrists have found occupational therapy to be an essential part of a therapeutic program, particularly for hospitalized patients Occupational therapy may also take the form of pre-occupational training as a part of adequate rehabilitation of injured persons

The medical literature, however, is extremely deficient in case studies and progress reports on occupational therapy Basic research, consisting of kinesiology studies and investigation of muscular-skeletal pathologic conditions, is also inadequate This sort of research is needed, together with studies aimed at evaluating certain crafts and shopwork activities, with the object of analyzing the motions required and their adaptability to applied kinesiology Familiarity with the present knowledge of technics and their effects should lead to further employment of this therapeutic agent and stimulate necessary studies

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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### CASE 32191

#### PRESENTATION OF CASE

A seventeen-year-old schoolgirl entered the hospital because of fever and swelling of the ankles.

At the age of three years, following an attack of acute appendicitis, the patient developed migratory polyarthritides, a heart murmur and chorea. She was kept in bed for six months, then allowed up on slightly restricted activity. When she was seven years old there was a second bout of migratory polyarthritides, of unknown duration, without recurrence of chorea. There were no cardiovascular symptoms. After the second attack she continued in good health until six months before admission, when she twisted her right leg while swimming. Soon afterward the right leg became painful from the knee down. A chiropractor manipulated the leg and the pain disappeared. A week or two later she caught a "head cold," without a sore throat but associated with a temperature of 100°F and a two-day bout of sharp pain in the left upper quadrant of the abdomen. One month later (five months before admission) she was admitted to a hospital with fever that was immediately relieved by sulfadiazine and penicillin. Two months before admission she was sick again, this time at home in bed with fever, muscle aches, cough and swollen ankles. After three weeks she was able to walk

about but continued to have fever and ankle edema, which disappeared with rest. The night before admission she developed nausea, vomiting and a "stomach-ache," which persisted until she entered the hospital.

On physical examination there was a patchy erythema over the abdomen. The left border of the heart was 12 cm. to the left of the midline, with the maximal impulse in the fifth interspace. There was an apical systolic thrill. The mitral first sound was forceful, followed by a blowing Grade IV systolic murmur. The pulmonic second sound was greater than the aortic. The lungs were clear. The tip of the spleen was palpable and nontender, but the liver was not felt. There were two punctate, red, nontender areas on the cushion and tip of the left thumb.

The temperature was 99.6°F, the pulse 94, and the respirations 18. The blood pressure was 130 systolic, 80 diastolic.

The red-cell count was 3,470,000, with 82 gm of hemoglobin. The white-cell count was 21,700, with 82 per cent neutrophils. There was a slight trace of albumin in the urine, and the sediment contained 2 red cells and 25 white cells per high-power field. In the chest film the heart appeared normal except for enlargement of the left auricle posteriorly, best demonstrated fluoroscopically. The electrocardiogram was normal. The sedimentation rate was 145 mm per minute (normal, less than 0.35 mm).

During the first three hospital days the temperature steadily rose to 104°F and then spiked to 103 or 104 daily for a week. Blood cultures on the second and third days were negative, but five out of eight taken during the hospital stay were positive for an alpha-hemolytic streptococcus of the Lancefield Group A type. With the rise in fever an unproductive cough came on, which was accompanied by a "stitch" in the left side and was sometimes intensified by inspiration.

By the fourth day a ground-glass density had appeared in the chest film, which obliterated the left half of the diaphragm and the left costophrenic

sinus, as well as the left border of the heart and lower half of the left chest. The heart was displaced to the left (Fig 1). The cardiac pulsations were vigorous. The spleen was not palpable. A few alpha-hemolytic streptococci grew in the throat culture. On the ninth day a macular rash appeared on the arms and backs of the hands and knuckles. On the thirteenth day the temperature peak was 100°F, and it was never any higher from that time on. Signs of fluid in the left chest gradually disappeared. There was no fever from the fourteenth to the eighteenth day. About the eighteenth day

appeared over the left chest posteriorly. The white-cell count was 20,000, with 73 per cent neutrophils, 13 per cent lymphocytes and 14 per cent monocytes. The legs and thighs were normal. The temperature and pulse did not change.

On the following evening the patient suddenly clutched the left upper abdomen, vomited and began writhing and groaning. She was pale, cold and sweating. The breath sounds were equally good on both sides, but dullness persisted at the left base. The trachea was not displaced. The heart sounds were rapid and regular, and the mur-

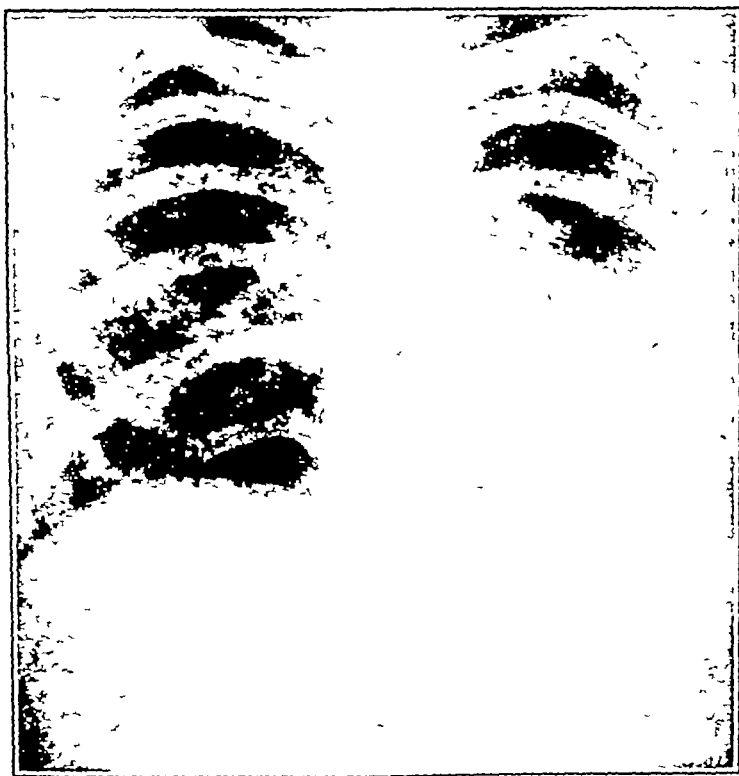


FIGURE 1 *Roentgenogram of Lung.*

she began to complain of a dull constant ache in the muscles of the right thigh anteriorly, interrupted by occasional sharp pains in that region. On the twentieth day she complained of nausea, anorexia and periumbilical discomfort. The blood penicillin level on the twenty-fourth day was reported to be at least 0.06 but less than 0.24 units per cubic centimeter. The organism was inhibited in vitro by 0.06 units of penicillin per cubic centimeter. On the thirty-third hospital day the patient noticed aching pain in the left epigastrium and midepigastrium. It was similar to the attack four weeks previously, being constant and questionably aggravated by respiration. There was mild tenderness in the left upper quadrant. Dullness again

was unchanged. The abdomen was quite silent, but at one time fairly normal peristalsis was heard. The abdomen was negative for fluid, spasm and tenderness. The knee jerks were hypoactive but equal. The patient was using both arms and both legs equally well in twisting and turning. She responded to questions by grunting. Oxygen slightly improved the color of the skin. Death occurred thirty minutes after the onset of this acute episode.

#### DIFFERENTIAL DIAGNOSIS

DR ALFRED KRANES There can be little doubt that this patient was suffering from subacute bacterial endocarditis, and I find it very difficult to

consider seriously any other disease in the differential diagnosis. We shall start the discussion then by assuming that this patient had subacute bacterial endocarditis. Certainly the presence of long-continued fever, anemia, muscle and joint pains and splenomegaly — at least I assume that the spleen was enlarged, although it was felt only on admission — occurring in a patient whose heart was previously damaged by two attacks of rheumatic fever is a reasonable background for assuming that the patient had bacterial endocarditis. When, in addition, five blood cultures are positive for alpha-hemolytic streptococci the diagnosis seems well-nigh conclusive. There are, to be sure, several findings frequently found in the disease that were not encountered here, but their absence argues little, if any, against it. No mention is made of clubbing of the fingers or of petechiae, unless one assumes that the two punctate hemorrhages on the left thumb were petechiae.

The disease probably began five or six months before admission, when she first complained of pain in the right lower leg, although that, of course, may have been a mechanical strain from swimming. On the other hand, people with bacterial endocarditis frequently have bizarre muscle and joint pains. The former are usually of embolic origin, resulting in muscle ischemia and pain. Certainly the disease was well advanced when she began to run a fever and complain of pain in the left upper quadrant, approximately five months before entry. As for the course of the disease, I see little worth commenting on at length. The episodes described are quite typical of bacterial endocarditis. Rashes are infrequent in the disease, but they do occur. Possibly it may have been a drug rash due either to penicillin or to something else, but rashes occur without the use of drugs in bacterial endocarditis. I think without much question that the repeated episodes of pain in the left upper quadrant can be ascribed to infarction of the spleen. It is such a common occurrence in the disease that I see no reason for trying to explain it on any other basis. The periumbilical pain, with nausea and anorexia, that persisted for a few days may have been due to an embolus in one of the small mesenteric vessels, too small to produce infarction of the bowel but large enough to produce a temporary disturbance of bowel function. The only findings worth commenting on are those in the left thorax. I think that it would be helpful to look at the x-ray films.

DR JAMES R LINGLEY This is a film taken on admission. The heart shadow is not appreciably enlarged in the transverse diameter, but it is enlarged across the base, owing to enlargement of the left auricle. It has a rather typical mitral configuration. The lungs were clear at that time.

DR KRANES Have you any hesitation in saying that it was a rheumatic heart?

DR LINGLEY That was our interpretation.

DR KRANES That is not quite clear from the record.

DR LINGLEY I remember it particularly because I interpreted the films myself. This film was taken four days later and one month before death and shows a marked change on the left. There is extensive density in the left lower lung field, with elevation of the diaphragm and displacement of the heart shadow to the left. The appearance is consistent with atelectasis of the left lower lobe, and there apparently is some fluid along the axillary border. The amount of atelectasis is not inconsistent with an infarct.

DR KRANES Can a high diaphragm itself produce that degree of atelectasis?

DR LINGLEY I do not believe so. I think that the elevation of the diaphragm is due to a collapse of the left lower lobe.

DR KRANES Before seeing the films I had visualized a somewhat different state of affairs. I had the impression, from the abstract, that most of the findings in the chest were explained by fluid, despite the statement that the heart had been displaced to the left. Consequently I had postulated that what was taking place was probably a large infarction of the superior pole of the spleen, as a result of which an inflammatory process had taken place, the spleen becoming adherent to the under surface of the diaphragm, with consequent irritation and outpouring of fluid into the pleural cavity. According to Dr Lingley, however, this looks more like a process going on within the lung itself. If that is so, one would have to assume that the infarction was pulmonary rather than splenic. I hesitate to make that diagnosis since in doing so one has to assume that the vegetations were on the right side of the heart — a rare occurrence in bacterial endocarditis. The overwhelming majority of vegetations occur either on the mitral or aortic valve, or both. Only infrequently are they found on the tricuspid or pulmonary valve from which pulmonary emboli would originate.

This raises another interesting question. Did this patient have rheumatic heart disease or are the findings described here compatible with a congenital heart of some sort? I think that one has a right to raise that question, despite the history of two attacks of rheumatic fever. The first attack, which occurred at the age of three and during which time the heart murmur was heard, may be seriously questioned. Although rheumatic fever does occur in children below the age of four or five it is extremely rare. When one hears a heart murmur at that age, even in the presence of chorea, one has a right to ask whether the murmur might not have been present previously. There is no way of answering that question in this case. The type of congenital lesion that might explain this would be, of course, a patent interventricular septum, and the findings on admission of a thrill and a loud

systolic murmur are not inconsistent with such a diagnosis. I am, however, inclined to believe the history and to accept at its face value the statement that two attacks of rheumatic fever occurred, particularly since the configuration of the heart, as pointed out by Dr. Lingley, was also consistent with rheumatic heart disease.

The real problem in this case centers around the nature of the terminal episode. What caused this patient's death within a period of thirty minutes after she had been apparently progressing quite satisfactorily? The usual causes of sudden death in patients with bacterial endocarditis are the result of emboli to various vital organs—the brain, the heart or one of the viscera. So far as the brain is concerned, there certainly is no evidence in this terminal picture on which to incriminate the central nervous system, although it is the most frequent site of embolism. They have been extremely explicit in telling us that the patient moved her arms and legs while thrashing around in bed.

So far as the heart is concerned it is somewhat more difficult to exclude a massive myocardial infarct as a result of occlusion of one of the coronary arteries by a vegetation. It is not an infrequent cause of sudden death in cases of bacterial endocarditis and is due either to large vegetations growing over the aortic valve and occluding one of the coronary mouths or to the breaking off of a small vegetation, which lodges inside a coronary artery. Although it is a perfectly possible situation that cannot be excluded, it is rather unlikely because of the clinical findings. The description of this episode does not sound like an attack of acute myocardial infarction. Although it does not specifically state so, I am assuming that the patient had a good deal of pain in the left upper quadrant. The only evidence is that she grasped that area. The record does not state that she had pain, but it is reasonable to infer that there must have been a good deal of pain. Pain localized to the left upper quadrant seems to me unusual in a patient dying of myocardial infarction. If that were the case, one would expect to hear some alteration in the quality of the heart sounds, but they are described as unchanged, aside from an increase in rate. I think that a large myocardial infarct from an occluded coronary vessel is not probable, although I cannot rule it out.

Nor can I exclude a pulmonary embolus. If these previous findings in the chest were due to pulmonary infarcts, the terminal event might also have been due to the same process, but again the clinical picture is not that of a pulmonary embolus. One learns, however, in these exercises that typical clinical pictures are rare. She was described as pale and sweating rather than cyanotic. Furthermore, after a month of therapy with penicillin, if any vegetations did persist, one would not expect them to be large. The pulmonary infarcts that occur with bacterial endocarditis are likely to be

small, not the massive ones that cause death. One must, of course, consider the possibility that the embolus arose from thrombi in a leg vein, but there was no evidence of phlebitis except for the pain in the right leg several weeks earlier. I am rather inclined to believe that this patient did not have a pulmonary embolus, although clinically such a diagnosis is somewhat more acceptable than is myocardial infarction.

Another unusual and rare cause of sudden death in bacterial endocarditis is rupture of an aortic valve due to ulceration secondary to the vegetative process. I do not see how we can make that diagnosis here. The usual picture is that of rapidly progressive congestive heart failure, as well as the occurrence of a diastolic murmur that had not previously been present. We are specifically told that no change occurred in the pre-existing murmurs, and under the circumstances a ruptured aortic cusp is extremely improbable.

Could this patient have had an embolus to one of the abdominal viscera? If so, to what viscus? I do not see how an embolus to any of the abdominal viscera usually involved could produce death in thirty minutes. It takes time for infarction of the bowel and perforation with peritonitis to occur. It would be a most unusual state of affairs for a patient with mesenteric thrombosis to die within so short a period. Had it taken place over a period of hours, I should consider it much more seriously.

One would like, of course, to tie up this terminal episode with what had gone before. The patient had complained several times of discomfort in the left upper quadrant, which I assume was due to infarction of the spleen. At the end she suddenly grasped the left upper quadrant, apparently in great pain. I should like to believe that the terminal episode had something to do with the spleen. If so, the only conceivable explanation that I can offer is a spontaneous rupture of the spleen. Certainly the clinical picture as given here fits that much better than anything else I can think of. I hesitate to mention it because it is so rare. It occurs in a variety of septic spleens and in leukemia. Although I am not aware of its having been described in bacterial endocarditis, I know that it has been reported in many other conditions in which the spleen has been septic or infarcted, such as in malaria. Certainly, if this were a case of malaria and the patient suddenly grasped the left upper quadrant and died in thirty minutes with signs and symptoms of shock or hemorrhage, there would be no doubt in one's mind that the patient died of a ruptured spleen. Possibly I have become sensitized to this condition after having seen one case of malaria with a ruptured spleen and a picture not dissimilar to this. It seems to me that the diagnosis of the terminal event lies essentially between pulmonary embolus, which is far more frequent but does not fit the clinical picture too well, and spontaneous

rupture of the spleen, which is rare but fits the description here better than anything else I can think of. So I shall suggest that

DR F DENNETTE ADAMS Could the lung picture have been due to ordinary collapse of the lung without infarction in a sick patient lying in bed?

DR KRANES As the terminal event?

DR ADAMS No

DR LINGLEY It would be unusual to have that amount of fluid with collapse

DR. DONALD S KING The symptoms of writhing and groaning interest me. I have never seen that picture with a pulmonary embolus. The patient with a pulmonary embolus is usually quiet and does not writhe. I think Dr Kranes's suggestion that it was due to something else is a good one.

DR BENJAMIN CASTLEMAN Dr FitzHugh, I believe that you saw this patient. Will you say a word or two about your impression?

DR GREENE FITZHUGH First, I want to congratulate Dr Kranes on his excellent discussion. We thought that the symptoms in the left upper quadrant were due to infarction of the spleen or left

## ANATOMICAL DIAGNOSES

Subacute bacterial endocarditis mitral valve  
Splenic infarcts, with rupture of spleen  
Hemoperitoneum  
Rheumatic heart disease, with mitral and aortic involvement  
Embolitic nephritis, healing  
Hydrothorax, left  
Pulmonary atelectasis left lower lobe  
Gluteal abscesses

## PATHOLOGICAL DISCUSSION

DR CASTLEMAN At autopsy, when the abdominal cavity was opened, we found the entire left side filled with clotted blood. The blood was present

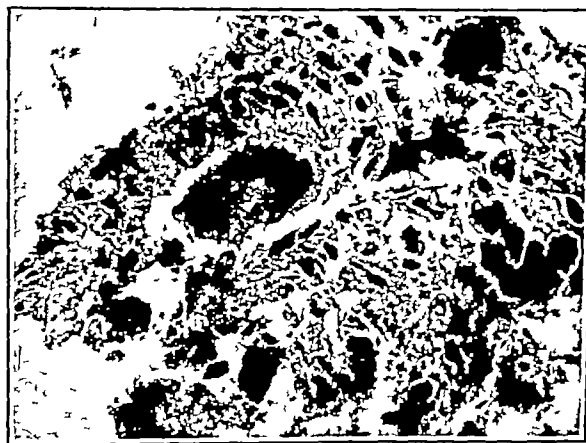


FIGURE 2 Photomicrograph of a Healing Bacterial Vegetation on the Mitral Valve

The dark-staining masses are clumps of cocci. Note the giant cell



FIGURE 3 Photomicrograph Showing a Healing Process in the Upper Portion of a Glomerulus

kidney. The spleen was felt by only one person out of the six or eight who examined her. I was not that one. We believed that she was having repeated infarcts. The lungs were negative.

## CLINICAL DIAGNOSES

Subacute bacterial endocarditis  
Pulmonary embolus

## DR KRANES'S DIAGNOSES

Subacute bacterial endocarditis  
Splenic infarcts  
Spontaneous rupture of spleen

in both the lateral gutter and the pelvis, but it was particularly concentrated in the region of the hilus of the spleen. There were infarcts in both the upper and the lower poles of the spleen. Between them, just anterior to the hilus, was a tear with a reddish-black clot over it. The spleen was about three to four times normal in size, weighing 640 gm. Most of the enlargement was probably due to the large amount of intrasplenic hemorrhage, which formed a clot measuring about 10 cm in diameter. This hemorrhage was adjacent to both the upper and lower infarcts, we were not certain that the hemorrhage began in either of these infarcts, although it probably did. There was no evidence of infarction in the central portion of the spleen.

The heart was only slightly hypertrophied. There was slight thickening of the aortic valve, but no evidence of bacterial endocarditis. The mitral valve was markedly thickened, and on one of the leaflets was a hard vegetation 2 or 3 mm in diameter, superimposed on which was a thin layer of friable



tissue. Clumps of organisms could be seen microscopically within the vegetation, with a lot of scarring and granulation tissue around them. In one granulating area we found a giant cell of the foreign-

was fairly adherent to the diaphragm. Dr. Kranes's initial hypothesis was therefore correct. The infarct had broken down and had irritated the diaphragm and pleura, thus producing pleural effusion



FIGURE 4 Photomicrograph Showing the Necrosis and Foreign-Body Giant-Cell Reaction at the Site of the Injection of Penicillin in Beeswax and Peanut Oil

body type (Fig 2). The process, therefore, was almost healed but still contained many organisms.

The kidney showed evidence of a healing embolic nephritis. About one fifth or one sixth of the glomeruli were involved, in some there was complete involvement, but in most of them only a small portion of the tuft was infarcted (Fig 3). There was no evidence of an acute embolic nephritis; all the lesions were healing or healed, which is fairly good evidence that no further emboli were getting into the kidney. This patient had been receiving penicillin in beeswax and peanut oil, and a section of the buttocks, where the injections had been given, showed fairly extensive muscle degeneration, surrounded by a foreign-body reaction (Fig 4). I should think that this might have caused a lot of pain.

DR. KRANES: Was there any evidence of pulmonary infarcts?

DR. CASTLEMAN: In the left lower chest there was 200 cc. of clear, straw-colored fluid, with surrounding atelectasis of the left lower lobe. There was no evidence of infarction. The splenic infarct in the upper pole was cystic, and before sectioning felt as if it might have been an abscess. This had extended to the capsule of the spleen and

and atelectasis. The pleural effusion had disappeared for the most part by the time of autopsy. This last x-ray (Fig 1) was taken one month before death.

## CASE 32192

### PRESENTATION OF CASE

*First admission.* A fifty-eight-year-old housewife entered the hospital during an acute asthmatic attack.

About twenty-five years before admission the patient had her first attack of bronchial asthma. There was no known precipitating event. Subsequently she had mild intermittent attacks for three or four years. Then she inhaled vapors from boiling hemlock branches and had a complete remission for fifteen years. Four years before admission, at the age of fifty-four, following an emotional upset she was again stricken by an asthmatic attack. After that there were infrequent mild attacks until ten months before admission, when she had an attack severe enough to require treatment by a doctor. Her next severe attack brought her to the hospital.

On physical examination there was labored, wheezing respiration, with a prolonged expiratory phase. The anteroposterior diameter of the chest was increased. The lung fields were hyper-resonant, the diaphragm was depressed, and expansion diminished.

The temperature was 99°F, the pulse 110, and the respirations 22. The blood pressure was 160 systolic, 110 diastolic.

The red-cell count was 5,360,000, and there were 15 gm of hemoglobin. The white-cell count was 10,950, with 62 per cent neutrophils and 9 per cent eosinophils. The urine was normal. By x-ray examination the lung fields were bright. The diaphragm was low, and its excursion limited. The pulmonary markings were prominent throughout the chest, particularly at the bases. The heart was slightly enlarged to the left. Orris powder caused a 2-cm skin wheal, with a 1-cm erythematous border. Chicken feathers, ragweed and goose feathers also gave positive, although smaller, skin reactions.

The asthmatic attack responded to aminophylline, ephedrine and sedatives. The patient was discharged on the third hospital day.

*Final admission* (twenty-eight months later). Within the next two years there were seven brief admissions for asthma. All were completely or partially relieved by aminophylline, chloral hydrate and potassium iodide. Between admissions the patient was sometimes free of asthma, but she often had attacks that required adrenalin injections by a doctor or visiting nurse. There was a general trend toward chronic asthma, with gradual shortening of the periods of good health. After several of the admissions she spent one or two weeks in a nursing home. During her third admission she had a pneumonia affecting the right lower lobe, and a Type 3 pneumococcus was isolated from the sputum. At the end of the two-year period she carried on fairly comfortably by taking potassium iodide, aminophylline and ephedrine daily. There was never any evidence of heart failure, and an electrocardiogram on the next to the last admission was normal. The chest films showed little change in the two years.

Two weeks before the final admission she began to have more frequent attacks, particularly at night. They gradually became worse, until finally nothing relieved them.

Physical examination revealed slight cyanosis and moderate respiratory distress. Expiratory wheezes and rhonchi were heard over both lung fields but were more numerous on the left. The heart sounds were faint. The pulmonic second sound was greater than the aortic. The neck veins were not distended. There was no enlargement or tenderness of the liver, nor any ankle edema.

Twenty-four hours after admission the patient's condition was considerably improved under the usual treatment of 10 cc of aminophylline intravenously. While dressing to go home, she suddenly

became much worse. When examined a few minutes later, she was seated half dressed in a chair, doubled forward and breathing in short grunts. The usual asthmatic rales were heard at the right base posteriorly, but the respiratory exchange was very shallow. She was extremely cyanotic. Oxygen was given by mask, and artificial respiration was started as the breathing was reduced to an occasional gasp. There were several convulsive movements of the face, and she died ten minutes after the onset of the attack.

#### DIFFERENTIAL DIAGNOSIS

DR J EVARTS GREENE. Here is another case in which the cause of sudden death is the chief problem. We know that this woman had asthma and that it began twenty-five years before admission, at the age of thirty-three years. She had a little trouble for three or four years, and then the inhalation of hemlock vapor "cured" her. At the age of fifty-four, following an emotional upset, she again developed asthma. This brings up the possibility of a reflex or nervous factor in the precipitation of asthmatic attacks, and apparently this patient did have asthma in response to emotional stimuli.

Physical examination on the first admission gave good evidence of emphysema. The anteroposterior diameter of the chest was increased, the lung fields were hyper-resonant, the diaphragm was depressed, and its expansion was diminished. At that time the blood pressure was 160 systolic, 110 diastolic, which indicates that she probably had some hypertension.

The laboratory work did not show a marked increase of red cells or hemoglobin, so that it does not appear that she had any compensatory polycythemia. The x-ray film of the chest was said to show prominent pulmonary markings, particularly at the bases. The heart was slightly enlarged to the left, and there was a question whether she had pulmonary fibrosis. The patient did obtain relief by coming to the hospital on frequent occasions. It is possible that she was sensitive to some dust at home, which was avoided when she came to the hospital.

She had Type 3 pneumococcus pneumonia on one of her admissions. In our experience pneumococcal pneumonia is infrequent in patients with bronchial asthma. Of course, it can and does happen.

Two weeks before the final admission, the attacks increased in frequency and severity. On entry she was slightly cyanotic and musical rales and rhonchi were heard, more numerous on the left side than on the right. There was no evidence of myocardial failure; the neck veins were not distended and there was no enlargement of the liver or edema of the ankles. Apparently no moist rales were heard in the lungs. Presumably no x-ray film of the chest was taken at the onset of the terminal event, which only lasted ten minutes. Perhaps we should see the x-ray films.

DR. JAMES R. LINGLEY We have films over a two-year period, which show practically the same thing, except for the pneumonia. This is the first film, and it shows marked emphysema on both sides, with slight enlargement of the heart on the left. This is the last film, taken two years later, and it shows practically no change.

DR. GREENE Is there any appreciable sign of fibrosis?

DR. LINGLEY There may be a moderate degree.

DR. GREENE Then we come to the terminal event, which lasted only ten or fifteen minutes. The cause of sudden death is difficult to determine. I do not feel entirely satisfied with any of the various possibilities that I think should be considered. The first is that this patient died simply of a bad attack of asthma, which came on for no obvious reason just as she was getting dressed to go home. Perhaps it was in response to the exertion of getting dressed, or perhaps there was an emotional basis in the thought of going home. Asthmatic attacks do develop suddenly under these conditions. On the other hand, a ten-minute period is extremely short for death from an attack of bronchial asthma, and apparently she had been fairly comfortable just before the terminal event. Cases have been described in which asthma led to death within an extremely short period of time.<sup>1</sup> I believe it is possible that this patient's death was based purely on asthma, although it is unlikely.

The second possibility that comes to mind is a massive pulmonary embolus. I cannot recall having seen fatal pulmonary embolism in patients with asthma. We have no evidence from the history that there was any focus from which a pulmonary embolus might have come, but there is no reason why she may not have had a large embolus from a femoral or pelvic vein.

A third possibility, coronary thrombosis, seems quite unlikely. There is no mention that the patient had pain. The main complaints seem to have been dyspnea and cyanosis, so that although coronary thrombosis is possible, I believe that it is unlikely.

A fourth possibility is spontaneous pneumothorax. A few cases have been described in which asthmatic patients have had spontaneous pneumothorax followed by death,<sup>2</sup> but they are exceedingly rare. If such had occurred one would expect the patient to have had a good deal of pain, and there should have been typical signs of pneumothorax, with shifting of the heart and the mediastinum to the opposite side. On the other hand, the description of the examination of the chest during the terminal episode is not at all complete, and we cannot be quite sure about the shift of the mediastinum, or whether the intercostal spaces were larger on the one side than on the other.

The fifth and final possibility is massive collapse of the lung, which may be due to sudden obstruction

of the bronchi, to pulmonary infarction, to infection, of which we have no evidence, to an allergic cause or to nervous stimuli. Again there should have been, unless the massive collapse was bilateral, shift of the mediastinum, although this time toward the affected side, and a high diaphragm on the same side.

Finally, I might mention just for the sake of completeness the fact that some patients with asthma die following the administration of morphine. We have no indication that this patient had been given morphine. Death has also been due to periarteritis nodosa and asthma, but there is no evidence that this patient had periarteritis nodosa.

Granted that none of the explanations that I have offered for the terminal episode are entirely satisfactory, I favor a diagnosis of pulmonary embolism in this case, particularly because of the sudden onset and the rapid course of the terminus, but also because the patient was making some exertion in the act of getting dressed, perhaps the first she had made in some hours, which could have led to the dislodging of a large thrombus in a femoral or pelvic vein.

#### CLINICAL DIAGNOSIS

Bronchial asthma  
Pulmonary embolus?  
Pulmonary emphysema

#### DR. GREENE'S DIAGNOSES

Bronchial asthma  
Pulmonary emphysema  
Hypertension  
Massive pulmonary embolism

#### ANATOMICAL DIAGNOSES

Bronchial asthma  
Spontaneous pneumothorax, left  
Pulmonary emphysema  
Cor pulmonale

#### PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN The autopsy findings in the usual case of a patient dying of an asthmatic paroxysm have often been described at these exercises by Dr. Mallory, and we have had 18 such cases out of a series of autopsies on 50 asthmatic patients. The lungs are usually ballooned and meet in the midline, covering the heart. They do not collapse when the chest plate is removed. On section, the bronchi are filled with mucous plugs, usually in the medium-sized bronchi, although occasionally in the large bronchi. The walls of the bronchi are thickened, and the mucous glands are hypertrophied. The basement membrane is thickened, and there is lymphocytic and eosinophilic cellular infiltration of the walls. Autopsy of this patient

On physical examination there was labored, wheezing respiration, with a prolonged expiratory phase. The anteroposterior diameter of the chest was increased. The lung fields were hyper-resonant, the diaphragm was depressed, and expansion diminished.

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## COMING ANNUAL MEETING

FOLLOWING an enforced hiatus of two years the one hundred and sixty-fifth anniversary of the Massachusetts Medical Society will be held at the Hotel Statler, Boston, on May 21, 22 and 23, the program of the meeting appears elsewhere in this issue of the *Journal*.

The first general session will begin at 2:00 p.m. on May 21 and comprises seven papers of general interest. Late that afternoon there will be a meeting of the supervising censors, followed in the evening by the annual meeting of the Council.

On the following morning, following four papers on miscellaneous topics, the annual meeting of the

Massachusetts Medical Society will be held, the annual oration to be given by Dr. Frank H. Lahey. The afternoon session begins with five papers of general interest and ends with the Shattuck Lecture, which will be given by Colonel John B. Youmans, M.C., A.U.S., chief, Nutrition Branch, Office of the Surgeon General, and professor of medicine, Vanderbilt University School of Medicine, the title being "Nutrition and the War." The annual dinner of the Society will be held that evening, the president, Dr. Reginald Fitz, will preside, the guest speakers being Dr. Roger I. Lee, president of the American Medical Association, and Dr. Elmer S. Bagnall, past president of the Society.

The program for the morning of the third day lists three papers of general interest and a symposium on bleeding from the gastrointestinal tract. At noon, the various sections will hold luncheon meetings, at each of which a short talk will be given on an appropriate topic. The meeting will conclude with the afternoon session, the program consisting of seven papers on miscellaneous topics.

The scientific and technical exhibits will be larger than ever before. Tremendous advances in the diagnosis and treatment of disease were made during the war years, and many of these are now being made available to the general practitioner for the first time. For this reason all the exhibits, particularly the technical ones, deserve the close attention of those who attend the meeting.

The usual continuous motion-picture program is scheduled for the second and third days.

An interesting schedule has been arranged for the wives of members, including attendance at the Pop Concert at Symphony Hall on the evening of the first day. A golf tournament for members will be held at the Wollaston Golf Club on the afternoon of the second day.

The Committee on Arrangements, which is composed of Dr. Roy J. Heffernan, chairman, and Drs. G. Guy Bailey, Jr., Harold G. Giddings, Robert L. Goodale and Sidney C. Wiggan, has set forth a program that should appeal to the returned veteran and to the general practitioner, and it seems likely that all previous records of attendance will be shattered.

showed all these findings in the lungs, but in addition, when the chest plate was removed, a large puff of air came out of the left chest and the left lung was found way over to the right against the spine. She undoubtedly had, as Dr. Greene mentioned, a pneumothorax. We have here then a combination of two conditions—the type of lung that is found in an asthmatic paroxysm and a pneumothorax. I believe that the latter was probably the precipitating cause of death. This is the first case of pneumothorax as a complication of an asthmatic paroxysm that we have had.

DR. RACKEMANN: I should like to ask Dr. Lingley if he would look at the x-ray films again to see if he

can find an emphysematous bleb. Why did the lung rupture?

DR. LINGLEY: There is no visible evidence of a bleb in this film.

DR. CASTLEMAN: The left lung showed two or three emphysematous blebs, but we were unable to find a definite tear. There was a moderate degree of emphysema throughout the lung, and definite hypertrophy of the right ventricle.

#### REFERENCES

1. Rackemann, F. M. *Clinical Allergy, Particularly Asthma and Hay Fever. Mechanism and treatment*. 617 pp. New York: Macmillan Company, 1931. P. 421.
2. Faulkner, W. B., Jr., and Wagner, R. J. Fatal spontaneous pneumothorax and subcutaneous emphysema in asthmatic: report of case with bronchoscopic findings. *J. Allergy* 8: 267-272, 1937.

## MEDICOLEGAL ABSTRACT

**Regulation of Practice by Government Unauthorized practice.** The defendant was a licensed cosmetologist and operated a "clear-skin" institute. He was charged with practicing medicine without a license in violation of Michigan Comp Laws 1929, Paragraphs 6743 and 6745. A jury found him guilty, and he appealed. The judgment was affirmed. The evidence showed that the complaining witness was suffering from acne and that the defendant, for a fee, undertook to treat her and did treat her by means of applying ointment and extracting blackheads. A physician qualified as an expert on skin diseases testified that papular acne "ordinarily spoken of as pimples," was a disease a physician without special training in dermatology would find difficult to differentiate from secondary syphilis and that it would certainly require a physician to treat it. There was some other evidence that the defendant engaged in the practice of medicine in violation of the statute — *People v Gilbert* 312 Mich 320, Oct. 8, 1945.

This case, however, is particularly interesting because it calls attention to the exceedingly broad provisions of the Michigan statute under which the conviction was obtained. Paragraph 6743 of the Comp Laws of 1929 makes it a misdemeanor to practice medicine without a license. Paragraph 6745 defines the practice of medicine as the actual diagnosing, curing or relieving in any degree, or professing or attempting to diagnose, treat, cure or relieve any human disease, ailment, defect or complaint, whether of physical or mental origin, by attendance or advice or by prescribing or furnishing any drug, medicine, appliance, manipulation or method, or by any therapeutic agent whatsoever. One has no need to be a lawyer to see how sweeping would be a literal construction of the provision making it criminal "to relieve by advice any human complaint of mental origin."

Although a chiropractor is not under Michigan law a physician or surgeon (*Erdman v Great Northern Life Ins Co*, 253 Mich 579), he is licensed under other provisions of the statute so that he can practice medicine — *Locke v Ionia Circuit Judge*, 184 Mich 535 and *People v Lewis*, 233 Mich 240. Similarly pharmacists are separately licensed. Although nurses are not specially licensed in Michigan they would seem to be within the principle that treatment given under supervision and direction of a doctor is not in violation of the statute — *In re Carpenter's Estate*, 196 Mich 561. The practice of midwifery alone, not accompanied by any other practice of medicine and surgery, is also excluded by interpretation.

Other limitations are not so clear. In *Locke v Ionia Circuit Judge*, 184 Mich 525, at 539, the court said

This sweeping effort at denunciation, with all provisions otherwise taken into account would render criminal numerous gratuitous and humane acts of relief and kindness to the suffering common amongst mankind in all ages and places. The police power of the state, though comprehensive, is scarcely adequate to compass the possibilities of such a definition, and it is difficult to discern in the title of the act any warning of a purpose to make such definition a part of the law of this Commonwealth.

In *People v Watson*, 196 Mich 34, the court said that some acts covered by the language of the statute might be innocently done. The assumption that things so done would not be in violation of the statute is clear. The meaning of things "innocently done" is not so clear. Certainly no criminal intent or *mens rea* is required to constitute the crime penalized by the statute. The court did, however, refer with approbation to the exception of "gratuitous and humane acts" made above. The notion that the statute would be limited to those who engage in the practice of medicine for gain and as a vocation is further strengthened in *People v Eckelyn*, 217 Mich 341. The nature of the acts done, however, would seem to be much more relevant than the question of whether they were done for charity or for pay. Thus, performing an appendectomy is practicing medicine even when done for charity, while consoling a widow could hardly be so considered even if were done in pursuit of a vocation.

Despite the broad language of the act there are extremely few cases under it, limitation in its meaning apparently depending primarily on the good sense of the prosecuting authorities.

## MISCELLANY

## PASSANO FOUNDATION AWARD

Selection of Dr Ernest W Goodpasture, professor of pathology and dean of the School of Medicine of Vanderbilt University, Nashville, Tennessee, as the 1946 recipient of the Passano Foundation Award is announced by the Board of Directors of the Foundation. Presentation of the \$5000 cash award will be made at an appropriate ceremony in Osler Hall of the Medical and Chirurgical Faculty of Maryland, in Baltimore, on the night of May 15. The Foundation, which was established in 1944 by the Williams and Wilkins Company, of Baltimore, proposes to aid in any way possible the advancement of medical research, especially research that bears promise of clinical application. For the encouragement of such research the Foundation has established the award as one of its activities. Following the presentation of the award by Mr Edward B Passano, chairman of the Board of Directors of the Williams and Wilkins Company, Dr Goodpasture will deliver an address entitled, "Research and Medical Practice." Dr Goodpasture receives the award for his original development of the method for propagation of viruses in pure culture by inoculation of chick embryos and for his outstanding contributions to advancement of knowledge of the cell-parasite relation in bacterial and viral infections.

## DR O'HARA APPOINTED DEAN AT TUFTS

Dr Dwight O'Hara, of Waltham, who is president-elect of the Massachusetts Medical Society, has recently been appointed dean of Tufts College Medical School. Dr O'Hara has been professor of preventive medicine at the school for a number of years and has been acting dean for the past four years, in the absence of Dr A Warren Stearns, who served as a captain in the Medical Corps of the United States Navy. Dr Stearns has been made head of the newly created Department of Applied Sociology at the Tufts School of Liberal Arts.

## THE INADEQUACIES OF MEDICAL CARE

### V HOW THEY CAN BE CORRECTED

THIS final editorial summarizes the suggestions made in the previous editorials concerning the correction of existing inadequacies of medical care. These comments will not be listed according to particular aspects but according to the agency that is responsible for their accomplishment.

The Government should promote an economy that guarantees good wages and a high standard of living, including adequate housing and transportation facilities. It should establish grants-in-aid to states in which there is demonstrated need for facilities concerned with the health of the people, incidentally, this could best be accomplished by the creation of a national department of health, headed by a secretary of Cabinet rank. Through an extension of the Social Security Act it should provide compensation for loss of wages due to sickness. Finally, it should organize, supervise and support a scheme for the continuance of co-ordinated medical research.

State governments should take the necessary steps, statutory or otherwise, to assure the licensing of well trained physicians, to eliminate improper medical practice by cultists, to improve hospital standards, to guarantee the necessary funds for the care of the indigent and to encourage an increase in nursing personnel through the licensing of attendant nurses. They should construct and equip hospitals and health centers in areas of demonstrated need and, if necessary, should employ or subsidize physicians in these institutions, all with the assistance of federal grants-in-aid. They should educate the public concerning matters of diet, accepted methods of preventive medicine and available facilities for medical care.

Medical schools should pay more attention to the need for training physicians who qualify as general practitioners rather than as specialists.

Both national and state medical societies should sponsor comprehensive programs for postgraduate medical education. State medical societies should assist state departments of health in educating the public regarding preventive medicine and available medical facilities, chiefly through the medium of

district and local health councils, and should promote plans for the assistance of those physicians who have had a substandard education.

Physicians should keep themselves professionally "fit" and should limit their practice to cases for which they are qualified to care. In certain instances, they should consider the advantages offered by group practice.

The number of hospital beds must be increased, and as a temporary expedient, hospitals should make full use of existing facilities. If necessary, they should improve equipment and personnel to meet accepted minimum standards. They should seriously consider the advisability of establishing affiliated convalescent homes.

All these things would do much to improve the health of the people, *but* they would not appreciably lower the cost of medical care. In other words, people must still insure against the expense of catastrophic illness, and the mere fact that they do has little to do with assuring good medical care. Indeed, a healthier Nation can only result from the combined efforts of a variety of agencies — governmental and otherwise. For this reason there seems to be little excuse for maintaining that a nation-wide system of compulsory health insurance is the *only* solution to the problem. It is true that such a scheme would solve one of the difficulties, — equalization of the costs of medical care, — but at the same time it would seriously handicap, if not abolish, many existing enterprises that are gradually accomplishing the very things that contribute to the improvement of medical care. Such enterprises, particularly voluntary schemes for prepayment medical-care insurance, should be encouraged and promoted by the medical profession and by the public, and they should be supported by states, cities and towns, if necessary through federal grants-in-aid.

## MASSACHUSETTS MEDICAL SOCIETY

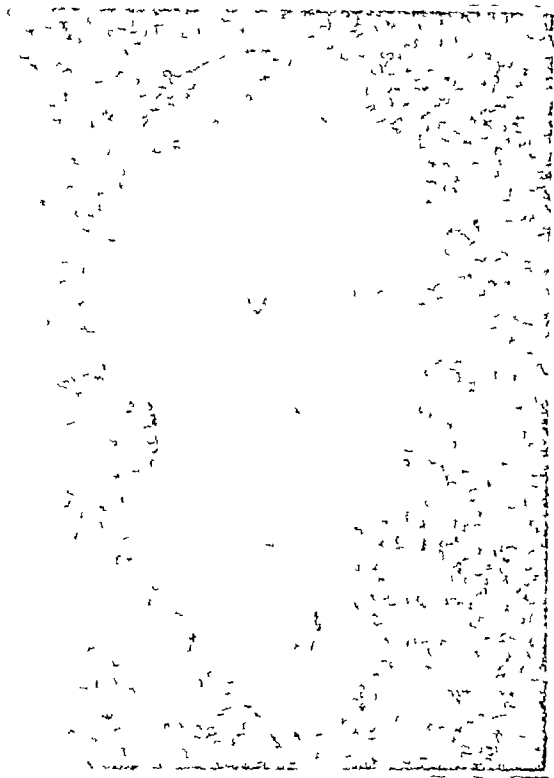
### DEATH

FESSENDEN — Charles H. Fessenden, M.D., of Newton, died April 19. He was in his eighty-third year.

Dr. Fessenden received his degree from Boston University School of Medicine in 1886. Until his retirement ten years ago, he had been for many years an x-ray specialist at Newton Hospital.

His son, two grandchildren and two great grandchildren survive.





## OFFICERS OF THE MASSACHUSETTS MEDICAL SOCIETY, 1945—1946

DR. DWIGHT O'HARA, *President-Elect**Bachrach*

- 2.25 *Results of Bilateral Suprardiaphragmatic Splanchnicectomy for Arterial Hypertension* DR. MAX A PEET, Ann Arbor, Michigan Professor of surgery, University of Michigan, chief, Neurosurgical Unit, University Hospital
- 2.30 *Delayed Chemical Pneumonia* DR. HARRIET L HARDY, Boston Physician to Division of Occupational Hygiene, Department of Labor and Industries, Commonwealth of Massachusetts, assistant in medicine, Massachusetts General Hospital
- 3.15 *Diabetes in Massachusetts* DR. ELLIOTT P JOSLIN, Boston Medical director, George F. Baker Clinic, New England Deaconess Hospital
- 3.40 *Surgical Problems in the Management of a Diabetic Patient* DR. LELAND S. MCKITTRICK, Boston Surgeon-in-chief, Palmer Memorial Hospital, visiting surgeon, Massachusetts General Hospital
- 4.00 *The Shattuck Lecture: Nutrition and the War* COLONEL JOHN B. YOUNG, M.C., A.U.S. Chief, Nutrition Branch, Office of the Surgeon General, Washington, D. C., professor of medicine, Vanderbilt University School of Medicine
- 1:00-5:00 *Annual Golf Tournament* (WOLLASTON GOLF CLUB, QUINCY, MASSACHUSETTS) — DR. JOSEPH H. CAREY, Chairman

### WEDNESDAY EVENING, MAY 22

- 7:00 *Annual Dinner of the Massachusetts Medical Society* (GEORGIAN ROOM)

#### Presiding

DR. REGINALD FITZ, president, Massachusetts Medical Society

#### Guest Speakers

DR. ROGER I. LEE, president, American Medical Association

DR. ELMER S. BAGYALL, past-president, Massachusetts Medical Society

*Ladies are cordially invited to attend the dinner*

*Tickets for the dinner must be procured in advance of the meeting*

### THURSDAY MORNING, MAY 23

#### Fourth General Session

##### GEORGIAN ROOM

DR. ARCHIBALD MCK. FRASER, *Chairman*

DR. ARTHUR J. GORMAN, *Co-chairman*

- 9:00 *The Hospital as a Center of Education* DR. WALTER G. PHIPPS, Salem Chief of the Surgical Service, Salem Hospital
- Discussers* DR. H. QUIMBY GALLUPE, Waltham and DR. CHARLES F. WILINSKY, Boston

- 9:25 *The Initial Care of the Injured* DR. GORDON M. MORRISON, Boston Chairman, Massachusetts Fracture Committee, American College of Surgeons

### Symposium: Bleeding from the Gastrointestinal Tract

- 9:50 *Gastrointestinal Bleeding: Diagnostic and therapeutic considerations* DR. CHESTER M. JONES, Boston Physician, Massachusetts General Hospital, clinical professor of medicine, Harvard Medical School
- 10:15 *Surgical Aspects of Hemorrhage in Peptic Ulcer* DR. GEORGE HEUER, New York City Professor of surgery, Cornell University Medical College, surgeon-in-chief, New York Hospital
- 10:40 *The Position of the Roentgenologist in Handling Patients Bleeding from the Gastrointestinal Tract* DR. RICHARD SCHATZKI, Boston Radiologist, Massachusetts General Hospital
- 11:15 *Question-and-Answer Period*
- 11:30 *Comparative Uses of Pentothal Sodium in Military and Civilian Practice* DR. RALPH M. TOVELL, Hartford, Connecticut Director of anesthesia, Hartford Hospital DR. CHARLES BARBOUR, member of staff, Hartford Hospital

THURSDAY NOON, MAY 23

### Section Meetings and Luncheons

12:00 M — 2:00 P M

*Tickets for all luncheons must be purchased in advance*

#### Section of Medicine

PARLOR B, HOTEL STATLER

DR. ALBERT A. HONOR, Boston *Chairman*

DR. DANIEL J. ELLISON, Lowell, *Vice-chairman*

DR. FRANCIS C. HALL, Boston, *Secretary*

- An Informal Talk on Heart Disease, Stressing Facts We All Want to Remember* DR. WILLIAM D. STROUD, Philadelphia Professor of cardiology, University of Pennsylvania Graduate School of Medicine, associate in medicine, University of Pennsylvania School of Medicine, cardiologist to the Pennsylvania Hospital

#### Section of Surgery

SALLE MODERNE, HOTEL STATLER

DR. CHARLES F. TWOMEY, East Lynn, *Chairman*

DR. ALEXANDER J. A. CAMPBELL, Boston, *Secretary*

- The Preoperative and Postoperative Care of the Surgical Patient* DR. OWEN H. WANGENSTEEN, Minneapolis Chief, Department of Surgery, University of Minnesota Medical School

#### Section of Pediatrics

THE JUNIOR LEAGUE, ZERO MARLBOROUGH STREET

DR. FLOYD R. SMITH, Pittsfield, *Chairman*

DR. GERALD N. HOFFEL, Cambridge, *Secretary*

- The Use and Abuse of Endocrine Therapy in Children* DR. NATHAN B. TALBOT, Brookline Assistant physician, Children's Medical Service, Massachusetts General Hospital

#### Section of Obstetrics and Gynecology

PARLOR A, HOTEL STATLER

DR. ARTHUR F. G. EDGELOW, Springfield, *Chairman*

DR. WILLIAM J. McDONALD, Boston, *Vice-chairman*

DR. GEORGE VAN S. SMITH, Brookline, *Secretary*

# PROGRAM OF THE ONE HUNDRED AND SIXTY-FIFTH ANNIVERSARY OF THE MASSACHUSETTS MEDICAL SOCIETY

Tuesday, Wednesday and Thursday, May 21, 22 and 23, Hotel Statler, Boston

The Registration Desk will be located on the Mezzanine Floor, and all who attend the meeting are requested to register

Owing to the lack of personnel and food supplies, the Hotel Statler must be informed concerning the number of members who will attend the various luncheons and dinners. Attendance is not limited, but tickets *must* be obtained in advance.

Members of the Society who are not councilors may obtain tickets for the Pop Concert on Tuesday evening by purchasing them (\$1.50 each) from Society Headquarters, 8 Fenway, Boston 15, *on or before May 15*. Their wives and friends are cordially invited to attend.

## TUESDAY AFTERNOON, MAY 21

### First General Session

#### GEORGIAN ROOM

DR. RALPH R. STRATTON, *Chairman*

DR. CARL BEARSE, *Co-chairman*

- 2:00 *Foreign Bodies in the Respiratory Tract* DR. JOHN R. RICHARDSON, Boston Assistant surgeon, Massachusetts General Hospital and Massachusetts Eye and Ear Infirmary, bronchoscopist, Massachusetts Eye and Ear Infirmary
- 2:25 *The Problem of Venous Thrombosis and Pulmonary Embolism* DR. JOHN HOMANS, Boston Clinical professor of surgery (emeritus), Harvard Medical School
- 2:50 *Anal Pruritus* DR. NEIL W. SWINTON, Waban Surgeon, Lahey Clinic and New England Deaconess and New England Baptist hospitals
- 3:15 *Anoxia Neonatorum* DR. CHARLES L. SULLIVAN, Chestnut Hill Assistant obstetrician, Massachusetts General and Saint Elizabeth's hospitals
- 3:40 *Progress — Penicillin Inhalation Therapy* DR. MAURICE S. SEGAL, Boston Assistant professor of medicine, Tufts College Medical School, junior visiting physician, Boston City and Beth Israel hospitals
- 4:05 *Functional Gastrointestinal Disorders: Lessons learned from military medicine* DR. JAMES A. HALSTED, Dedham Assistant physician, Massachusetts General Hospital
- 4:30 *Tuberculosis Case Findings* DR. JOHN A. FOLEY, Boston Director 5th and 6th Medical Services, Boston City Hospital, chief of staff, Boston Sanatorium, clinical professor of medicine, Boston University School of Medicine. DR. JOHN B. ANDOSCA, Boston Instructor in medicine, Boston University School of Medicine

- 5:00 Supervising Censors' Meeting (PARLOR D)
- 6:00 Cotting Supper for Councilors (PARLORS A AND B)

## TUESDAY EVENING, MAY 21

- 7:00 Annual Meeting of the Council (GEORGIAN ROOM)
- 8:30 Pop Concert (SYMPHONY HALL)

## WEDNESDAY MORNING, MAY 22

### Second General Session

#### GEORGIAN ROOM

DR. W. JASON MIXTER, *Chairman*

DR. CHARLES J. E. KICKHAM, *Co-chairman*

- 9:00 *Some Observations on the Recent Food Rationing Program* DR. JOSEPH GARLAND, Boston Physician to the Children's Medical Department, Massachusetts General Hospital
- 9:25 *The Diagnosis and Treatment of Infective Hepatitis* DR. WILLIAM C. MOLONEY, Boston Assistant professor of clinical medicine, Tufts College Medical School, visiting physician, Carney and St. Elizabeth's hospitals
- 9:50 *Tropical Diseases in World War II Returnees* CAPTAIN JAMES J. SAPERO (MC), U.S.N., Washington, D.C.
- 10:15 *Streptomycin* DR. CHESTER S. KEEFER, Boston Director, Evans Memorial, Massachusetts Memorial Hospitals, physician-in-chief, Massachusetts Memorial Hospitals
- 11:00 Annual Meeting of the Massachusetts Medical Society (GEORGIAN ROOM)
- Annual Oration (following annual meeting) Gastric Surgery DR. FRANK H. LAHEY, Boston Director, Lahey Clinic, surgeon-in-chief, New England Deaconess and New England Baptist hospitals
- Annual Luncheon (PARLORS A, B AND C) tickets must be procured in advance of the meeting

## WEDNESDAY AFTERNOON, MAY 22

### Third General Session

#### GEORGIAN ROOM

DR. ELMER S. BAGNALL, *Chairman*

DR. JOHN FALLON, *Co-chairman*

- 2:00 *Medical Aspects of Hypertension* DR. NORMAN A. WELCH, Boston Clinical professor of medicine, Tufts College Medical School, physician-in-chief, Carney Hospital

2.25 *Results of Bilateral Supradiaphragmatic Splanchnicectomy for Arterial Hypertension* DR MAX A PEET, Ann Arbor, Michigan Professor of surgery, University of Michigan, chief, Neurosurgical Unit, University Hospital

2.50 *Delayed Chemical Pneumonitis* DR HARRIET L HARDY, Boston Physician to Division of Occupational Hygiene, Department of Labor and Industries, Commonwealth of Massachusetts, assistant in medicine, Massachusetts General Hospital

3.15 *Diabetes in Massachusetts* DR ELLIOTT P JOSLIN, Boston Medical director, George I Baker Clinic, New England Deaconess Hospital

3.40 *Surgical Problems in the Management of a Diabetic Patient* DR LELAND S MCKITTRICK, Boston Surgeon-in-chief, Palmer Memorial Hospital, visiting surgeon, Massachusetts General Hospital

4.00 *The Shattuck Lecture Nutrition and the War* COLONEL JOHN B YOUNG, MC, AUS Chief, Nutrition Branch, Office of the Surgeon General, Washington, D C, professor of medicine, Vanderbilt University School of Medicine

1.00-5.00 *Annual Golf Tournament* (WOLLASTON GOLF CLUB, QUINCY, MASSACHUSETTS) — DR Joseph H Carey, Chairman

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#### Guest Speakers

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DR ARTHUR J GORMAN, *Co-chairman*

9.00 *The Hospital as a Center of Education* DR WALTER G PHIPPEY, Salem Chief of the Surgical Service, Salem Hospital

*Discussers* DR H QUIMBY GALLUPE, Waltham, and DR CHARLES F WILINSKY, Boston

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10.40 *The Position of the Roentgenologist in Handling Patients Bleeding from the Gastrointestinal Tract* DR RICHARD SCHATZKI, Boston Radiologist, Massachusetts General Hospital

11.15 *Question-and-Answer Period*

11.30 *Comparative Uses of Pentothal Sodium in Military and Civilian Practice* DR RALPH M TOVELL, Hartford, Connecticut Director of anesthesia, Hartford Hospital DR CHARLES BARBOUR, member of staff, Hartford Hospital

THURSDAY MORNING, MAY 23

#### Section Meetings and Luncheons

12.00 M — 2.00 P M

*Tickets for all luncheons must be purchased in advance*

#### Section of Medicine

PARLOR B, HOTEL STATLER

DR ALBERT A HONOR Boston, *Chairman*

DR DANIEL J ELLISON Lowell, *Vice-chairman*

DR FRANCIS C HALL, Boston, *Secretary*

*An Informal Talk on Heart Disease, Stressing Facts We All Want to Remember* DR WILLIAM D STROUD, Philadelphia Professor of cardiology, University of Pennsylvania Graduate School of Medicine, associate in medicine, University of Pennsylvania School of Medicine, cardiologist to the Pennsylvania Hospital

#### Section of Surgery

SALLE MODERNE, HOTEL STATLER

DR CHARLES F TWOMEY, East Lynn, *Chairman*

DR ALEXANDER J A CAMPBELL, Boston, *Secretary*

*The Preoperative and Postoperative Care of the Surgical Patient*

DR OWEN H WANGENSTEEN, Minneapolis Chief, Department of Surgery, University of Minnesota Medical School

#### Section of Pediatrics

THE JUNIOR LEAGUE, ZERO MARLBOROUGH STREET

DR FLOYD R SMITH, Pittsfield, *Chairman*

DR GERALD N HOEFFEL, Cambridge, *Secretary*

*The Use and Abuse of Endocrine Therapy in Children* DR NATHAN B TALBOT, Brookline Assistant physician, Children's Medical Service, Massachusetts General Hospital

#### Section of Obstetrics and Gynecology

PARLOR A, HOTEL STATLER

DR ARTHUR F G EDGELOW, Springfield, *Chairman*

DR WILLIAM J McDONALD, Boston, *Vice-chairman*

DR GEORGE VAN S SMITH, Brookline, *Secretary*

*The Pathologist Looks at Abortion* DR ARTHUR T HERTIG, Boston Assistant professor of obstetrics and assistant professor of pathology, Harvard Medical School, pathologist, Free Hospital for Women and Boston Lying-in Hospital

### Section of Dermatology and Syphilology

HANCOCK ROOM, HOTEL STATLER

DR BERNARD APPEL, Lynn, *Chairman*

DR FENNER A CHACE, Fall River, *Secretary*

*Fatty Acid Treatment of Fungous Infections* DR SAMUEL M PECK, New York City Associate attending dermatologist, Mount Sinai Hospital, New York City

### Section of Anesthesiology

PARLOR C, HOTEL STATLER

DR SIDNEY C WIGGIN, Waban, *Chairman*

DR LEO V HAND, Newton, *Secretary*

*Progress in Anesthesia in the Veterans Administration* DR RALPH M TOVELL, Hartford, Connecticut Chief, Department of Anesthesiology, Hartford Hospital

### Section of Radiology

4TH FLOOR, HOTEL STATLER

DR GEORGE LEVENE, Chestnut Hill, *Chairman*

DR EDWARD B D NEUHAUSER, Cambridge, *Secretary*

*Encephalographic Studies of Patients with Head Injuries* DR RICHARD H SCHATZKI, in collaboration with DR DONALD H BAXTER and DR CHARLES E TROLAND

### Section of Physiotherapy

PARLORS D AND E, HOTEL STATLER

DR ARTHUR L WATKINS, Boston, *Chairman*

DR HOWARD MOORE, Boston, *Secretary*

*A Sound Moving Picture on Rehabilitation Entitled "Accident Service"* With a discussion by DR GEORGE C DEEVER, New York City, and DR ALEXANDER P AITKEN, Boston

## THURSDAY AFTERNOON, MAY 23

### Fifth General Session

GEORGIAN ROOM

DR FRANK R OBER, *Chairman*

DR HARRY BLOTNER, *Co-chairman*

2 00 *Some Current Trends in Obstetrics* DR SAMUEL A COSGROVE, Jersey City, New Jersey Clinical professor of obstetrics, Columbia University Faculty of Medicine, medical director, Margaret Hague Maternity Hospital, Jersey City, New Jersey

2 25 *Some Practical Aspects of Electroencephalography* DR RANDOLPH K BYERS, Boston Associate visiting physician, Children's Hospital, instructor in pediatrics, Harvard Medical School

2 50 *The Ulcer Problem* DR OWEN H WANGENSTEEN, Minneapolis Chief, Department of Surgery, University of Minnesota Medical School

3 15 *Skin Manifestations of Capillary Fragility Their Diagnosis and Treatment* DR SAMUEL M PECK, New York City Associate attending dermatologist, Mount Sinai Hospital, New York City DR ALFRED L COPLEY, research associate, Department of Biology, New York University

3 40 *Physical Rehabilitation of the Disabled* DR GEORGE C DEEVER, New York City Physician in charge of physical medicine, Bellevue Hospital, medical director, Institute for Crippled and Disabled

4 05 *A Discussion of Some Debatable Questions in the Treatment of Heart Disease* DR WILLIAM D STROUD, Philadelphia Professor of cardiology, University of Pennsylvania Graduate School of Medicine, associate in medicine, University of Pennsylvania School of Medicine, cardiologist to the Pennsylvania Hospital

4 30 *Blood Transfusions and Transfusion Reactions* DR WILLIAM DAMESHEK, Boston Professor of clinical medicine, Tufts College Medical School, hematologist, Pratt Diagnostic Hospital

### MOTION-PICTURE PROGRAM

- SALLE MODERNE

Wednesday, May 22

9 00- 9 40 *The Story of DDT*  
9 45-10 10 *Esophageal Diverticulum*  
10 15-11 00 *Hemothorax, Empyema and Specific Remedial Breathing Exercises* (courtesy of Dr D E Harken)  
3 00- 3 20 *Complete Neck Dissection*  
3 25- 4 05 *Combined Operation Fusion of lumbosacral joint*  
4 15- 5 00 *Foreign Bodies in the Lung and Mediastinum* (courtesy of Dr D E Harken)

Thursday, May 23

9 00-9 35 *Skin Grafting*  
9 40-10 10 *Aseptic Ileocolostomy*  
10 15-11 00 *Foreign Bodies in the Pericardium and Heart* (courtesy of Dr D E Harken)  
2 30- 3 00 *Cancer of the Female Breast*  
3 05- 3 25 *Subtotal Thyroidectomy*  
3 30- 4 00 *Physical Rehabilitation of the Disabled* (courtesy of Dr George C Deaver)

### SCIENTIFIC EXHIBITS

BALLROOM ASSEMBLY

BOOTH  
S-13 *Council of Dental Health Program* MASSACHUSETTS DENTAL SOCIETY  
S-14 *Modern Pharmacy* MASSACHUSETTS PHARMACEUTICAL ASSOCIATION  
S-15 *Blue Shield The doctors' voluntary plan* MASSACHUSETTS MEDICAL SERVICE.  
S-16 *Enuresis The use of cystourethrography in diagnosis* DR M LEOPOLD BRODNY AND DR. SAMUEL A. ROBINS

S-17	Anesthesia	THE MASSACHUSETTS MEMBERS OF THE NEW ENGLAND SOCIETY OF ANESTHESIOLOGY	Exhibitor Boston City Hospital	Certified Milk Producers Association	S-4
				Children Incorporated	9
S-18	Anesthesia	THE MASSACHUSETTS MEMBERS OF THE NEW ENGLAND SOCIETY OF ANESTHESIOLOGY	Exhibitor Beth Israel Hospital	Ciba Pharmaceutical Products, Inc	S-7
				Coca-Cola Company	13 & 14
S-19	Anesthesia	THE MASSACHUSETTS MEMBERS OF THE NEW ENGLAND SOCIETY OF ANESTHESIOLOGY	Exhibitor Massachusetts Memorial Hospitals	Crosbie-Macdonald	46
				Davies, Rose & Company	40
S-20	Industrial Dermatology	DEPARTMENT OF DERMATOLOGY, TUFTS COLLEGE MEDICAL SCHOOL.		Denver Chemical Mfg Company	M-24
S-21	Massachusetts Study of Child Health Services	AMERICAN ACADEMY OF PEDIATRICS	Exhibitor Dr Lendon Snedeker, deputy state chairman	Dobo Chemical Company	S-2
S-22	Anesthesia and Thyroid Surgery	THE LAHEY CLINIC	Exhibitors Dr U H Eversole and associates	Eaton Laboratories, Inc	M-25 & 26
S-23	Thyroidectomy in Thyroid Surgery	THE LAHEY CLINIC	Exhibitor Dr Elmer C Bartels	J H Emerson Company	S-12
S-24	Military Plastic Surgery	VALLEY FORGE GENERAL HOSPITAL.	Exhibitor Lieutenant Colonel Bradford Cannon, MC, A US, and Captain Joseph E. Murray, MC, A US	C B Fleet & Company	45
S-25	Tuberculosis Control	HEALTH DEPARTMENT, CITY OF BOSTON (Frederick J Bailey, M.D., Commissioner)		Gerber Products Company	43
S-26	Sterility	FREE HOSPITAL FOR WOMEN	Exhibitor Dr John Rock	J E Hanger, Inc	35
S-27	The First Two Weeks of Human Development	FREE HOSPITAL FOR WOMEN, AND CARNEGIE INSTITUTION OF WASHINGTON	Exhibitor Dr Arthur T Hertz	Hanovia Chemical Mfg Company	51
S-28	Blood Fractionation Program	THE MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH		H J Heinz Company	27
				Hoffmann-La Roche, Inc	29
				The Hygeia Nursing Bottle Company	M-21
				Hynson, Westcott & Dunning, Inc	17
				The "Junket" Folks	M-20
				Kalak Water Co of New York, Inc	S-9A
				The Kelley-Koett Manufacturing Company	7
				Kellogg Company	M-5
				Kidde Manufacturing Co, Inc	M-23
				Lederle Laboratories, Inc	57
				Lee De Forest Laboratories	32
				Libby, McNeil & Libby	20
				Eli Lilly & Company	38
				J B Lippincott Co	S-10
				M & R Dietetic Laboratories	16
				E F Mahady & Company	Stage
				Mead Johnson & Company	52 & 53
				Medical Protective Company	21
				Mellin's Food Company	31
				The Mennen Company	S-9
				William S Merrell Company	S-11
				The National Drug Company	1
				Nestle's Milk Products, Inc	M-4
				Nestle's Milk Products, Inc Food Sales Dept	M-28
				T J Noonan Company	M-18
				North American Philips Company	10
				Parke, Davis & Company	M-10
				E L Patch Company	15
				Pet Milk Sales Corporation	25
				Philip Morris Company, Ltd, Inc	49
				Rare Chemicals, Incorporated	M-22
				L & B Reiner	33
				Riedel-de Haen, Inc.	54
				Sandoz Chemical Works, Inc	42
				Schenley Laboratories, Inc.	S-8
				Schering Corporation	41
				G D Searle & Company	24
				Sharp & Dohme, Inc	50
				Smith, Kline and French Laboratories	8
				Spencer, Inc.	S-5
				E R Squibb & Sons	M-7
				Frederick Stearns & Company	47 & 48
				Surgeons & Physicians Supply Company	50
				Tailby-Nason Company	18
				Vaponefrin Company	6
				Walker Vitamin Products, Inc	M-27
				Westinghouse X-Ray Company	2 & 3
				White Laboratories, Inc.	36 & 37
				Winthrop Chemical Company, Inc.	55
				Wyeth, Incorporated	M-1, 2, 3
				F E Young & Company	26
				The Zimmer Company, Inc.	M-19

### TECHNICAL EXHIBITS

The booths without letters are in the Ballroom, those preceded by "S" are in the Ballroom Assembly, and those preceded by "M" are in the Meszanine

	BOOTH	
Abbott Laboratories	56	
Alkalol Company	22	
American Hospital Supply Corp	S-6	
Ames Company, Inc.	44	
Ayerst, McKenna & Harrison	19	
Chester Baker, Inc.	S-33	
Baker Laboratories	S-5	
Best Foods, Inc.	M-11	
Elzhuber-Knoll Corp	34	
Ernst Buehler Company	M-6	
The Borden Company	28	
Brewer and Company, Inc.	4 & 5	
Enstol Laboratories, Inc.	M-29	
Buffington's, Inc.	39	
Burroughs Wellcome & Company.	25	
Cambridge Instrument Company.	M-30	
Camel Cigarettes	11 & 12	
Carnation Company	M-12	

## CORRESPONDENCE

## MILITARY MEDICINE

*To the Editor* The writer of the editorial "Merger and Medical Service," which appeared in the March 28 issue of the *Journal*, has expressed some views which deserve further comment. It seems to me that, in advocating a merger of the medical services of all the armed forces, he has gone unnecessarily far out of his way to disparage military medicine as practiced during the recent international disagreement.

One's opinions on almost any subject are derived either from what he himself has experienced or from what he has read or heard of the experiences of others. If the gentleman who wrote this editorial served personally with the Medical Corps of the Army or Navy he has, of course, every right to express his views, however dim they may be, but if this is actually the case, I suggest that his experience differed considerably from that of the majority of medical officers. If his expressed opinions are based on hearsay, as he seems to imply, I submit that possibly he has listened too attentively to a vocal minority, many of whom have purely personal reasons for their dissatisfaction with military medicine.

Although I am not qualified to speak of medicine in the Navy or of Army medicine in the Asiatic-Pacific or Mediterranean theaters, forty-four months' experience as an Army medical officer in this country, England, France and Germany has brought me to the following conclusions, with which I believe that the vast majority of my former colleagues would agree.

Army medicine is in so many respects superior to civilian medicine that there is no legitimate basis for comparison. This is a sweeping generalization, but there are so many specific examples by which it can be substantiated that I hardly know where to begin. I should ask your editorialist to consider the incidence of typhus in the American army in the ETO, I should ask him what he thinks of the military policy of universal compulsory chest x-ray films on all personnel, I should ask him to cite a single civilian community where expert, free medical care, hospitalization and laboratory facilities are constantly available to anyone at any time, regardless of his social or economic status. Finally, I should ask this. If civilian medicine is so superior, why all the current agitation, from almost every quarter, to remodel it completely?

One frequently hears the statement, "Army medicine was fine, but only because so many civilian doctors joined the Army." The absurdity of this viewpoint becomes apparent when one considers that in time of war no department of the Army would be of much value if it were not for civilian soldiers. No one will maintain that Army medicine was perfect, we all saw situations that could have been improved (and usually were, in time), conditions requiring correction (they usually got it) and procedures that were carried out inefficiently (especially by inexperienced personnel, who later learned Army techniques). In my own personal experience, I never saw a "snafu" of any magnitude that was not the direct or indirect result of some former civilian's attempt to do things in his own—and often highly original—fashion, rather than in the time-tested and experience-proved Army way.

I do not understand exactly what your writer means when he speaks of medical officers being "treated as enlisted men." The statement is too vague for comment. When he states that they were "ordered to do menial duties," I should again like more details. I, myself, never saw this happen. I know many a former major or colonel who is not now above helping his wife with the after-supper dishes, none ever washed a plate in the Army. I wonder what the "menial duties" were, and who gave the orders.

If the writer of your editorial would accompany me to any local civilian hospital he cares to designate, I shall undertake to point out to him defects in cleanliness, sanitation and administration that would not be tolerated in an Army installation. He will probably see gum-chewing ward attendants, dirty food handlers, smoking in kitchens, orderlies in need of shaves or haircuts, dusty floors, unnecessary noise, grime under the radiators—but why go on?

Finally, one should consider the care of the patient. In the last analysis, this will always depend for its quality

on the character and qualifications of the doctors and nurses in attendance, and, to a lesser extent, on the amount and nature of the material, human as well as inanimate, that is available to assist them. Where but in the Army (or Navy) are to be found hospitals that combine all the following features: every nurse a graduate, every ward officer having completed at least one internship, and many, residencies, an almost unlimited supply of drugs, instruments, hospital furnishings and professional equipment of every type, a competent visiting staff actually in residence, expert consultants in every branch of medicine and surgery, always available, well trained, well disciplined ward personnel, laboratory, x-ray and other diagnostic facilities constantly at hand, with no restrictions on their legitimate use, the whole, at no cost to the patient, and in fact with economic considerations of any kind never a limiting factor.

Many of us who served with the forces deplore the currently fashionable tendency to indulge in the indoor sport of "knocking the Army." We resent it for a variety of reasons, but chiefly perhaps for these three:

We were there and know from our own observations that the over-all picture was superlatively good.

We do not understand how any civilian, however talented or however "vocal," can possibly be in a position to judge the quality of military medical care.

We observe, often to our own embarrassment, that the most virulent criticism almost invariably emanates from those who have purely personal grievances, whether real or imaginary, against the military system, one, perhaps, failed to get promoted, another was relieved of his command, a third is upset because "someone else got the Legion of Merit." This translation of personal and usually deserved misfortune into a blanket condemnation of the Army as a whole is as subversive and as unconstructive as it is in bad taste.

WINTHROP WETHERBEE, JR.

24 School Street  
Boston

\* \* \*

The editorial in question does not unqualifiedly condemn military medicine. It does, however, imply that mistakes were made and that much might be accomplished toward future improvement if these faults were acknowledged and attempts were made toward their correction. Unfortunately, the experiences of many of the medical officers, particularly those assigned to small medical units, were not so satisfying as those of Dr. Wetherbee and his associates.

It is extremely difficult and hazardous to compare military and civilian medical care, since the recipients of the former are controlled by a rigid system of discipline. On the other hand, it must be acknowledged that the majority of advances, particularly in peacetime, originate in the large teaching units, and the editorial suggests that one of the aims of a merged medical department might well be a closer affiliation with such units than has existed in the past. — Ed

## REPORT OF MEETING

## MASSACHUSETTS CENTRAL HEALTH COUNCIL

The annual meeting of the Massachusetts Central Health Council was held on April 9, 1946. At the business meeting, after reports for the year by the president and the secretary-treasurer, the following officers were elected for the ensuing year: president Dr. George C. Shattuck, vice-president Dr. Channing Frothingham, and secretary-treasurer Mr. Arthur J. Strawson.

The business meeting was followed by a discussion entitled "Symposium on Group Practice." The principal speaker was Dr. Kingsley Roberts, director of Medical Administration Service, Incorporated, New York City.

Dr. Roberts approached the subject from the angle of better distribution of good medical care. He believed that, however financed, medical care should be organized on a prepayment basis, that the unit for care should be the family and not the individual, that the plan should include care in the home as well as in the hospital, and that the use of preven-

\*The opinions expressed are those of the speakers. The Massachusetts Central Health Council has taken no position for or against group practice.



nive methods should be an essential part of the plan. To these ends, physicians should know more about socioeconomic matters and about how to persuade patients to take advantage of the periodic physical examination and of other means of conserving health. He added that some units offering group practice are well organized and that others are not. Certain of them offer only diagnostic, consultative or specialized services. Others offer service of a general character. For broad medical coverage, co-ordination of the work of the staff by a person who understands preventive as well as curative medicine is essential. Research should also be a function provided for in the budget.

The development of group practice, in the opinion of Dr. Roberts, is necessary to keep down cost, to promote the efficient distribution of medical care and to encourage the systematic application of preventive methods.

For the future, Dr. Roberts envisioned health centers in small communities, to be served by groups of physicians. A number of such health centers should be affiliated with a teaching and hospital unit in the nearest large city, and a flow of personnel back and forth between the teaching unit and the health centers should be provided for. Such a plan would not only improve medical service in small communities but it would also provide the participating physicians in such communities with an adequate income and educational advantages.

Dr. Roberts then contrasted several types of group practice that are now in operation and said that many medical veterans have been impressed with the advantages of group practice as it exists in the Army and have been asking advice about how to form or to join a group for practice in civil life.

The formal discussion was opened by Dr. Elmer S. Bagnall of Groveland. Dr. Bagnall deplored the fact that discussions of possible changes in medical organization too often are characterized by controversialism. He believed that discussions aimed at expanding the areas of agreement should continue to be held and that this approach would prove profitable. Although not a member of a medical group, Dr. Bagnall said that the problems of organizing group medicine are worthy of study. Because people in a democracy resent regimentation and insist on the right to make mistakes, he thought that change should be gradual and by evolution. As a means of further study of medical problems on a community basis, Dr. Bagnall added that the formation of local health councils should be further stimulated, and he pointed out that the Massachusetts Medical Society has been discussing a two-way system of arranging for hospital care through central hospitals and subsidiary hospitals. The importance of the general practitioner as the co-ordinating link between the patient and the various specialists was stressed.

Dr. Fallon, of Worcester, who has been practicing in a group for many years, emphasized the ease of consultation within the group and the fact that diverse opinions can be expressed with the utmost freedom. Usually, the patient gets the benefit of at least two viewpoints. Laboratory and x-ray examinations are facilitated. When the cost of x-ray examination exceeds a specified figure, the group bears the additional expense. The members of the group, although specially qualified in certain fields, perform general work as well, and the internist gets a more equitable remuneration than is usual when surgery is required.

He added that there are many obstacles to success in group practice. Consequently, many groups have survived for only a few years. Dr. Fallon said that he did not wish to see group medicine replace the family doctor, who alone can have intimate knowledge of the patient's background.

Dr. Parkhurst, of Beverly, a member of a medical group, expressed interest in the plans outlined by Dr. Roberts but thought that it would be a long time before such a plan could be put into successful operation. He and other members of his group see patients not only in the office but also in the home. The patient chooses his physician within the group, but the group does not attempt to replace the general practitioner. Since a group is only as good as the men behind it, it should be built on the basis of ability to give good service rather than be formed from the physicians who happen to reside in the same locality. In certain instances it may be necessary to bring in outsiders having special qualifications. He added that a well organized group can not only provide improved services to a community but it may also become the nucleus of an efficient hospital staff.

Dr. Lendon Snedeker, of Boston, who at present is engaged in a fact-finding survey of health services for children in

Massachusetts sponsored by the American Society of Pediatrics, said that Dr. Roberts' tentative plan is not unlike a scheme that is now in operation in Sweden, with private practice as an overlay. "Why, indeed," he said, "cannot a general practitioner who is the family counselor be the key man in a group?"

In closing, Dr. Roberts pointed out that his general plan can be and should be adapted to local needs and that he too was convinced of the need for the general practitioner.

## BOOK REVIEWS

*Neuro-Ophthalmology*, By Donald J. Lyle, M.D. 4<sup>th</sup> cloth, 395 pp. with 234 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$10.50.

This book, the first American text to cover overlapping territory in the fields of neurology and ophthalmology, should prove a useful reference summary for practitioners and teachers of neurology and ophthalmology. Material for the text has been derived from 130 case histories, in all but 4 of which the clinical diagnoses were verified anatomically. Seventy-one pages are given to over seventeen hundred references, alphabetically arranged. There are 234 black-and-white figures with 529 separate illustrations, diagrams or photographs.

Ophthalmologists particularly should be grateful to the author for portraying vividly by pen and picture the related neurologic and ophthalmologic aspects of intracranial lesions and for correlating the same by collateral anatomical diagrams and photomicrographs, x-ray photographs, visual fields and fundus photographs. One of the outstanding virtues of this work is that it brings to the ophthalmologist a neurologic point of view and a better understanding of visuomotor and visuosensory pathology.

Although the reviewer has only admiration for this important work, and faith that revision for the second edition will iron out the few rough spots, he wonders how the publisher could fail to include much of the preface and the first ten pages of Chapter I, whether the author would not consider it helpful to clarify the signs in supranuclear, nuclear, infranuclear and internuclear lesions affecting the third, fourth and sixth cranial nerves, and whether half the photographs of fundi should be replaced by more informative diagrams or photomicrographs of significant intracranial lesions.

*Clinical Roentgenology of the Digestive Tract*. By Maurice Feldman, M.D. Second edition. 8<sup>vo</sup>, cloth, 769 pp., with 551 illustrations. Baltimore: The Williams and Wilkins Company, 1945. \$7.00.

This book is largely a review of the older literature, giving major points in roentgenologic diagnosis and stressing their clinical application. For the student of roentgenology or of gastroenterology too many varieties of lesions, with rather questionable proof, are stressed. For the practitioner of either roentgenology or gastroenterology, however, the book should be an excellent reference source, so long as common sense is used in interpreting the extremely uncommon or doubtful types of lesions.

An excellent index and bibliography are included. The latter is divided, being appended at the end of each section, which makes it of particular value because of its ready accessibility.

*Peripheral Nerve Injuries: Principles of diagnosis*. By Captain Webb Haymaker, M.C., A.U.S., and Major Barnes Woodhall, M.C., A.U.S. 8<sup>vo</sup>, cloth, 227 pp., with 225 illustrations. Philadelphia: W. B. Saunders Company, 1945. \$4.50.

This book covers a field already well cultivated. The particular value of this publication lies, however, in the expert condensation and the unusual illustrations. The text is accurate and dependable, but the student or physician will gain most from a study of the photographs and drawings that accompany it. No previous publication on this subject is more clearly illustrated. Each maneuver of testing motion is not only described, but all phases of it are shown in the pen sketches. The book should appeal to a wide audience,

particularly medical students and physicians who practice neurology and neurosurgery. Printed on excellent paper, with clear type and a good binding, this book deserves the highest recommendation. It was widely distributed by the United States Army.

*The Falling Sickness. A history of epilepsy from the Greeks to the beginnings of modern neurology.* By Owsei Temkin, M.D. 4<sup>th</sup>, cloth, 380 pp., with 7 illustrations. Baltimore: Johns Hopkins Press, 1945. \$4.00.

Dr. Temkin, who is an associate professor in the Department of History of Medicine at Johns Hopkins University, writes on the history of epilepsy from the time of the earliest reference by the ancient Greeks to 1880, when the effect of the work of Hughlings Jackson and Charcot became incorporated into medical thought. Naturally, much of the material, particularly that dealing with the earlier periods, is extracted from works dealing with speculations found in the opinions of laymen, philosophers and theologians, as well as those of physicians. The disease was closely associated with magic, lunacy, theology and the literature surrounding such vague subjects as the supernatural and the occult. It was not until the beginning of the nineteenth century that epileptic patients began to be hospitalized and carefully observed. Charcot separated out the epileptic manifestations due to hysteria, and Jackson, the symptoms resulting from a focal lesion in the brain.

Dr. Temkin has covered the whole story in a skillful manner. References are given to every statement of fact. His style is meticulous, and the chapters are supplemented by an extensive bibliography and an excellent index. The book is a credit to American medicine in the historical field and should be of use to all historians and those physicians who have to deal with convulsive disorders.

*The Modern Medical World. Portraits and biographical sketches of distinguished men in medicine.* By Solomon R. Kagan, M.D. 8<sup>th</sup>, cloth, 223 pp., illustrated. Boston: Medico-Historical Press, 1945. \$6.00.

In this volume the author presents a series of admirable biographical sketches and portraits of three hundred and twenty medical men distinguished for their notable contributions to science from the beginning of the nineteenth century. A large proportion of the portraits are reproduced for the first time. The names are arranged not alphabetically but chronologically under groups of men working in identical fields. In this collection and publication Dr. Kagan makes a valuable contribution to the record of modern medical history.

*Microbial Antagonisms and Antibiotic Substances.* By Selman A. Waksman, M.S. and Ph.D. 8<sup>th</sup>, cloth, 350 pp., with frontispiece. New York: The Commonwealth Fund, 1945. \$3.75.

The chasms separating many of the fields of abstract and applied science are often as wide as that between science in general and the layman's understanding thereof. This is a book bridging one such void between the field of soil and water microbiology, where microbial antagonism is an old story, and practical medical science, where antagonism was, until recently, a forgotten one.

The first two chapters discuss soil and water micro-organisms and their interrelations. Taken as a group, these forms of life make up the oldest of all living associations. It soon appears that they also have their parasitic parvenues. In the third chapter the field narrows to a consideration of these. The medical reader may be somewhat startled to find that the author apparently favors classifying one of medicine's venerable D.A.R.'s, the leprosy bacillus, as a "facultatively parasitic soil organism." The field still further narrows, however, to include only those parasites which have developed mass-murder methods of a high order against their fellow microbes. The fourth chapter, replete with research suggestions and possibilities, outlines methods of finding and isolating these antagonistic organisms and of identifying and assaying their products.

The next five chapters cover the known antagonists and the antibiotic agents of five broad groups of micro-organisms — bacteria, actinomycetes, higher fungi, protozoa and viruses. The tenth chapter lists the thirty-odd antibiotic agents of note in the five broad groups and outlines what is known of their chemical composition. The eleventh discusses antibiotic action and distinguishes it from antiseptic action. The remaining chapters take up present applications and future possibilities.

The applied scientist usually likes his data in handy-reference form and may regret that each antibiotic substance is treated in so many places in the book. Many such readers could benefit from an example of thorough, if apparently digressive, treatment. Good balance is maintained in the handling of the various substances — none, not even the author's favorite, receiving undue consideration at the expense of the others.

The book provides the interested beginner with the technique and basic background needed for a start. At the very least it should give the conventional bacteriologist with his mania for pure-culture study something more exciting to look for than the discard-bucket when he finds bacterial and mold contaminants on his plates. The sixty-page bibliography will keep him from rushing into print with his first discovery.

## NOTICES

### ANNOUNCEMENTS

Dr. George L. Maltby announces the opening of an office at 29 Deering Street, Portland, Maine, for the practice of neurological surgery.

Dr. Philip S. Marcus, having returned from military service, announces the reopening of his office for the practice of anesthesiology at 270 Commonwealth Avenue, Boston.

Dr. H. Herman Shuman announces his return from military service and resumption of the practice of pediatrics at 34 Maple Street, Springfield.

Dr. Garrett L. Sullivan, having returned from military service, is resuming the practice of ophthalmology at 101 Bay State Road, Boston.

### NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular meeting of the New England Society of Physical Medicine will be held at the Ring Sanatorium and Hospital, Arlington, on Thursday, May 16, at 8 p.m. Dr. John G. Trump will speak on the topic, "High-Voltage X-Rays and Cathode Rays for Cancer Therapy."

### SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MAY 16

FRIDAY, MAY 17

\*9:00-10:00 a.m. Clinicopathological Conference. Drs. Stanley Bradley and H. E. MacMahon Joseph H. Pratt Diagnostic Hospital

\*10:00 a.m.-12:00 p.m. Medical Staff Rounds Peter Bent Brigham Hospital

MONDAY, MAY 20

\*12:15-1:15 p.m. Clinicopathological Conference Peter Bent Brigham Hospital

TUESDAY, MAY 21

\*12:15-1:15 p.m. Clinicoroentgenological Conference Peter Bent Brigham Hospital

WEDNESDAY, MAY 22

\*9:00-10:00 a.m. Hyperadrenocorticism Dr. Robert H. Williams Joseph H. Pratt Diagnostic Hospital

\*10:30-11:30 a.m. Medical Clinic Isolation Building Amphitheater Children's Hospital

\*12:00 p.m. Clinicopathological Conference (Children's Hospital) Amphitheater Peter Bent Brigham Hospital

\*2:30-4:00 p.m. Combined Clinic by the Medical Surgical and Orthopedic Services Amphitheater Children's Hospital

\*Open to the medical profession

MARCH 15-SEPTEMBER 15 Boston University Course for Discharged Medical Officers Page 240 issue of February 14

APRIL 1-June 1 Intensive Course in Ophthalmology Page 240, issue of February 14

MAY 6-11 American Board of Obstetrics and Gynecology Page 458, issue of March 28

(Notices continued on page xvii)

# The New England Journal of Medicine

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Volume 234

MAY 16, 1946

Number 20

## HEALTH BILLS PENDING IN CONGRESS\*

### Part One

FRANZ GOLDMANN, M D †

NEW HAVEN, CONNECTICUT

THE fight over a national health program is on. An unprecedented number of bills for the improvement and extension of health services is pending in Congress. We may be confused by this flurry of legislative activity and may differ in our opinions about the merits of these bills. But we may be said to be at heart on the side of any program designed to adjust the health services to the rapid progress of medical science and the profound socioeconomic changes that have taken place since the nineteenth century.

Naturally and inevitably, one question is immediately raised. Is there any need for a nation-wide health policy as contrasted to local development of health programs? To answer this question one must define the unmet needs.

### PUBLIC-HEALTH SERVICES

There is need for the extension and strengthening of the basic public-health services. Despite creditable achievements in the development of community-wide services designed to prevent illness and promote good health, the goal is far from being reached. Full-time health units are operating in less than two thirds of all counties, and many of these are without adequate staffs and sufficient funds. The annual per capita expenditure for local health work is \$0.61, whereas about \$1.00 would be necessary to meet at least the most urgent requirements, and \$2.00 to \$2.50 to meet them all. But the problem is not only one of allotting more money, its solution also requires a reorganization of administrative structure.

Historically, the responsibility for the administration of local health services has been vested in the city, town, village or township. Many of these units are too small in population or too weak in resources to employ the necessary full-time public-health personnel. After years of study, a committee of the American Public Health Association,<sup>1</sup> headed by Dr. Haven Emerson, has proposed a plan whereby the 3070 counties and their contained cities in the

United States can be served by 1197 units of local health administration. More than two thirds of these units would serve several counties. It is imperative to create service districts rather than to continue the administration of public-health services by small political units.

### FACILITIES FOR MEDICAL CARE

There is need for more hospital beds, for better distribution of the various types of hospitals and for improvement of the quality of many facilities for medical care. In response to an ever growing demand, the number of hospital beds in this country has increased from about 35,000 in the early 1870's to 1,729,945 in 1944, or from approximately 1 bed to more than 12 beds per 1000 population, although it must be borne in mind that some 550,000 beds are in federal hospitals restricted to certain groups.

Despite and because of this great progress, we must not rest on our laurels. There are shortcomings that ought to be eliminated. The over-all bed rate falls short of present standards. According to the prevailing opinion, 4.5 beds in general hospitals are necessary for every 1000 persons, but the actual rate is below 4.0. In mental hospitals 5.6 beds would be necessary, but only 4.6 beds are available. In tuberculosis hospitals there is need for 2 beds for every death from this disease, but there are available only 1.3 beds per death from tuberculosis. Obviously, a substantial number of additional beds must be provided to meet the requirements of the time. No illusion should be entertained about the magnitude of this task.

The distribution of the existing hospitals is extremely uneven. At present, the best supplied states have about three times as many hospital beds per 1000 population as do the states with the lowest bed rates, and this inequality is even greater when only the general hospitals are considered. Hospitals are located where money is abundant and where there is enough wealth to build them and enough purchasing power to pay for their services. The wealthier states comprise about one quarter of those in the Union. The poorer parts of the country, the

\*This is the first of a series of four lectures on medical sociology given at the Harvard Medical School during February and March 1946. They were sponsored by the Department of Preventive Medicine and were primarily intended for third year students.

†Associate clinical professor of public health, Yale University School of Medicine.

very regions undersupplied with hospital beds, have more need for modern treatment service

Certain types of facilities are conspicuous by their rarity. This applies primarily to chronic-disease hospitals and convalescent hospitals, which are necessary for the proper and humane care of the sick as well as for the effective and economical operation of general and special hospitals.

To place emphasis on the number rather than the quality of medical-care facilities would be to ignore a fundamental of hospital policy. The hospital at its best is a superb institution. Many hospitals meet the highest standards, but many others need to be improved, and hundreds of institutions in actual operation are hospitals in name but primitive infirmaries in fact. At present, approximately two thirds of all hospital beds are in hospitals approved by the American College of Surgeons as meeting the standards considered fundamental to good hospital care, and most of them are in the large cities. It is noteworthy that the American College of Surgeons excludes hospitals with less than 25 beds from inspection and approval. According to a special survey made in 1939, nearly one third of all registered and nonregistered facilities for medical care and more than one third of such general and related hospitals had fewer than 25 beds. In 1944, it was found that nearly one fifth of the hospitals registered by the American Medical Association had less than 25 beds. The excuse for the existence of such small facilities is that many of these hospitals offer the *only* inpatient service in small communities. All the facts point to the necessity of reorientation of hospital policy to assure high standards of care throughout the country.

The shortcomings mentioned have discouraged highly skilled physicians from settling in small communities and have induced those practicing in small communities to move to large cities at the earliest possible moment. They have deprived many a country doctor of easy access to a hospital and of the opportunity for intellectual growth and technical assistance.

Since the increase and expansion of hospitals have taken place without over-all planning, governmental and nongovernmental activities in the hospital field are unco-ordinated. They duplicate each other in some communities and are entirely lacking in others. What is needed is a nation-wide hospital policy devised, accepted and carried out by all groups concerned, and concerted action rather than isolated effort.

District health centers, although they are essential to successful public-health work, have just begun to develop. At present they are intended to attain a functional and administrative co-ordination of all local health activities by housing under one roof a variety of clinics and also certain bureaus for the administration of health work within districts. In connection with the formulation of plans for an in-

tegrated hospital system, the potential value of public-health centers to broad health programs has been the subject of much debate. It might be wise to develop the old-type district health centers into centers of both preventive health activities and medical care for the whole community by making them the headquarters of physicians and related groups in private practice as well as of personnel employed by public and private agencies.

#### DISTRIBUTION OF PHYSICIANS

There is need for better distribution of competent physicians and members of allied professions. The large majority of the physicians in actual practice are graduates of approved schools, but many of the older physicians have had little opportunity to do more than occasional post-graduate work. Early in 1942, about every fifth physician reported himself as a specialist, but only about 18,000 names were listed in the *Directory of Medical Specialists*.

There is a good deal of disagreement concerning what constitutes a satisfactory ratio of physicians to population. Before the war, there was one doctor in active practice for every 935 persons, and this ratio was unsurpassed by any other country. How many physicians will be needed in the future is problematical. The only experience gained relates to organized programs operating on the basis of full-time group practice. Some of these plans, rendering complete service, need one physician for 1000 persons and others one for every 1200. What is not known is the ratio of physicians to population under a broad health program operating on the basis of the individual practice of medicine. In estimating future demand, allowance must be made for full-time service by physicians in public-health work, for the administration of hospitals and clinics and medical-care programs and for special services, such as those of the Veterans Administration.

The distribution of physicians leaves much to be desired. At present, they are concentrated in densely populated areas, large urban centers and relatively rich sections of the country; they are rare, if not lacking, in thinly settled areas, small communities and relatively poor sections. As might be expected, the location of doctors in the past was primarily influenced by the purchasing power of the people in a given community and to some extent by the availability of good hospitals and social and educational advantages. Significantly, the largest number of physicians per unit of population was found in the sections of the country with the largest dollar amount of retail sales per capita. Equally significant is the fact that the accredited specialists, with negligible exceptions, are practicing in large communities with good hospitals.

#### ORGANIZATION OF PROFESSIONAL SERVICES

There is need for organization of professional services according to the requirements of the time.

With the rapid advance of scientific medicine, the sum total of knowledge and skill has become so great that it cannot be mastered by any single person. The family doctor loses his patients, since people expect more than before from the physician and tend to consult a specialist without first seeing the general practitioner. Inevitably a growing number of young physicians, for one reason or another, are anxious to specialize in one of the many narrowly bounded specialties and refuse opportunities to gain experience in general practice. All too often the patient is regarded as a mere aggregation of parts, seen only through an optical instrument, and is referred from one specialist to another without receiving the services of a physician. The following story written by a British physician,<sup>2</sup> speaks for itself.

The need for the general physician is illustrated in this true story of six specialists and no doctor. There was a man with inframammary pain who betook himself to a cardiologist, who suspected a spinal-cord lesion and sent him to a neurologist, who diagnosed *spinal osteoarthritis* and sent him to a radiologist whose x-rays revealed nothing. Being still in pain he went a little later to a chest specialist who discovered nothing but suspected a psychoneurosis and sent him to a psychiatrist who refused to get to work until the man had been to a clinical pathologist who reported that all blood examinations were normal. The patient returned to the psychiatrist and was still in conference with him when last heard of.

One is therefore justified in asking whether the wheels of history are to be turned back and specialization is to be curbed, or whether the family doctor shall be strengthened by being made the link between patient and specialist. The answer is clear. Effort must be concentrated on the smooth co-operation of general practitioners and specialists, so that the general practitioner can readily be the family doctor, the specialist can complement him as he ought to, and the patient can receive the optimum in quality, efficiency and economy of service. The wide recognition of the need for a new approach to the organization of professional services explains the current interest in the development of group practice of medicine.

It is high time to proceed to sound organization of more group-practice units of different types in large cities and smaller communities, so as to gain experience about the best method of organization and the potentialities and limitations of this form of medical practice.

#### EXTENT OF MEDICAL CARE

There is need for more and better treatment of disease and defects. Innumerable studies on this subject have appeared. A digest of statistical data fills a volume of more than two hundred pages.<sup>3</sup> The findings differ in detail but are alike in regard to the essential facts.

The extent to which medical care is actually received depends largely, although not only, on ability to pay. This is contrary to American ideals, which call for equal service to all according to need. In general, persons in the high-income brackets receive

relatively much more service — and in many cases better care — than do those in the middle-income and low-income groups, although the need for service tends to increase with decreasing income. The proverbial statement that the rich and the poor receive good service is correct with respect to those of the former who have chosen their parents well and consequently do not have to worry about their sickness bills and for those of the latter residing in large cities and for those living outside large cities when they need hospitalization.

Until a few years ago there was a large group of forgotten men and women — the self-supporting persons with low and moderate incomes. It is of great significance that the picture has begun to change since the development of voluntary health-insurance plans. There is accumulating a large body of evidence showing that the removal of the economic barrier between those ready to render service and those demanding medical care eliminates much of the inequality of service so typical of earlier times. A pertinent example is afforded by the experience of Blue Cross plans. The studies of the Committee on the Costs of Medical Care,<sup>4</sup> based on the famous investigation by Roger I. Lee and Lewis W. Jones, arrived at the conclusion that 107 admissions per 1000 population would be necessary to provide satisfactory hospital care. Actually, the average number of admissions among the 20,000,000 persons covered by Blue Cross plans is 107 per 1000 eligible persons. It should be borne in mind that the majority of the subscribers to the Blue Cross belong to the middle-income group and before the initiation of insurance programs received only half the amount of hospital care that they now obtain. Twenty million persons constitute only a fraction of the total population, however, and the situation in general leaves much room for improvement. According to the United States Public Health Service,<sup>5</sup> in 1942 the civilian population of the continental United States obtained in non-federal general and allied special hospitals care equivalent to 0.92 days per person. This compares with 1.4 days believed to be necessary. In Massachusetts, the number of days of hospitalization was 1.4 per person per year, but in Mississippi it was only 0.3.

The gap between the volume of service actually received and the standards of good medical care is much greater if service outside the hospitals is considered. In 1945, about 5,000,000 persons were enrolled in voluntary prepayment plans covering physicians' services and the majority were eligible for limited service only. In many rural areas and small communities professional service is received only in emergencies. In dental care, the extraction of teeth is the service most frequently performed, and conservation of the teeth and prophylaxis play a distinctly minor role.

The question of adequacy or inadequacy of medical care has been, and still is, the subject of heated

discussions. Some medical authors have consistently denied that there is much inadequate medical care. The results of the Selective Service examinations came as a shock to those who had been doubting Thomases, but did not surprise those who had closely studied the many surveys of health conditions in various economic groups and in urban and rural areas. By April, 1945, nearly 5,000,000 male registrants, or 30 per cent of those examined, had been classified as unfit for military service. Of the young women applying to the Women's Army Corps, over one third had been rejected because of physical and mental defects. As Dr. Roger I. Lee<sup>6</sup> has remarked, the figures are sobering. However one interprets these data, it is certain that the health conditions of these young men and women in the prime of life are nothing to be proud of. In this connection it deserves mention that a total of 1,500,000 young men inducted with defects were readily rehabilitated for military service, and this experience clearly proves that much can be achieved by providing for more and better medical care.

What, then, are the major reasons for the existing inequality of service? Many persons go without adequate medical care because they lack the money to pay for it and are unwilling to accept charity. Some do not seek it because they are not health-conscious or prefer to rely on the drug clerk, an almanac or the advice of the old woman next door. Still others do not desire the services readily available to them, believing that they will not get their money's worth. Everyone knows that there is illness and defect for which little can be done in the light of present knowledge, but it should be realized that there is also much illness and defect for which much could be done.

#### COST OF MEDICAL CARE

There is need for organization of group payment for medical care. Authors writing for popular consumption often refer to "the romance of medicine." The story of the advance of medical science does read like fiction, but unfortunately there is another side to this picture, hospital bills and doctors' charges are nonfiction.

The rise of scientific medicine has greatly increased available knowledge and skill and made medical care more efficient than ever. With this, medical care has become more complex and more expensive. Profound economic and social changes have had a strong bearing on need, demand and ability to pay for all the services that modern medicine has to offer, with the result that the gap has been widening between medical science and medical practice.

The actual medical expenditures of a large fraction of the population are insufficient for adequate care, and they are ill related to the actual needs. People spend primarily on such services as are

readily available and economize on those that cannot be easily obtained. They are inclined to make certain expenditures that would not be necessary to the same extent were there a complete program of medical care. Proportionately, medical-care expenditures do not figure largely in the total expenditures of the average family. The patient who has to carry the full burden of costs when they occur, however, finds neither consolation nor help in the knowledge that the average costs of medical care represent a small fraction of the expenditures of all families. What matters to him is that he has to pay for the service. Medical costs are unpredictable, unbudgetable and often unbearable. As the head of a family of four with a combined family income of \$1800 once remarked, "If I get sick I go broke paying the hospital and doctors. Then I worry so that I get sick again."

The full benefits of scientific medicine cannot be reaped unless available knowledge and skill are applied to all the people, and this implies the development of organized payment plans designed to make the costs of medical care predictable, budgetable and bearable. We cannot afford not to develop organized payment plans, because they serve the interests of all — the patients, the health professions, the hospitals and the Nation. The average expenditures of all families and individuals for medical care are fairly constant and in recent years have constituted 35 to 40 per cent of their incomes. The country as a whole spends 4 per cent of the national income on all health services. This money, if spent wisely, can buy more and better service for all.

#### DISABILITY

There is need for protection of the individual and the family against economic losses resulting from disabling illness. Serious disease brings with it not only high expenditures for professional and institutional services but also substantial losses in income, depletion of savings or both. As stated by a California Senate committee,<sup>7</sup> "Under the present system a siege of sickness brings many families to bankruptcy."

Provision of medical care alone cannot solve all the problems of the sick. Protection of the patient from want caused by reasons beyond his control is a fundamental function of any organized social order based on moral principles. Moreover, quick and thorough restoration of health can be accomplished only if the patient is able to maintain a reasonably fair standard of living during the time he is prevented from working and earning. Provision for the financial support of those temporarily disabled by illness must go with any medical-care program if waste of money and effort is to be avoided. Provision for persons with long-term disability is a necessary part of a comprehensive social-security program.

### MEDICAL RESEARCH

There is need for broad and deep research in medicine, its underlying sciences and its social use. In the past, research in the cause, prevention and treatment of disease depended largely on support from endowment income, gifts and foundation grants. Powerful indeed was the influence thus exerted on medical research, and great were the accomplishments of those research workers fortunate enough to obtain some modest support for important projects. But all too often long-term fundamental research in clinical medicine and the basic sciences had to be sacrificed for short-term and fragmentary research, if not solely for confirmatory studies or barren projects. Studies of prime importance had to be discontinued prematurely because of lack of money, whereas studies of secondary importance were carried on because they were financed by earmarked funds. Preoccupied with clinical studies, most of the medical schools neglected research in the socioeconomic aspects of illness and of medicine. Institutions other than the prominent universities found it difficult to develop adequate research programs. Many gifted research workers, unable to afford the financial and personal sacrifices expected of them, left institutions of higher learning to accept positions with industrial companies or other organizations willing to give them both the opportunity to concentrate on their chosen fields and the necessary implements.

As Dr Vannevar Bush<sup>8</sup> has said so well, "Further progress requires that the entire front of medicine and the underlying sciences of chemistry, physics, anatomy, biochemistry, physiology, pharmacology, bacteriology, pathology, parasitology, etc., be broadly developed." To this list one may add the socioeconomic and psychologic aspects of illness and the socioeconomic aspects of medicine.

The constant and rapid increase in the cost of medical research, coming at a time when the old sources of income are dwindling, has thrown the whole problem into sharp relief. The experience during the war has clearly shown how it can be brought closer to a satisfactory solution. It is now widely recognized that substantial support from tax funds is necessary if research in medicine, its underlying sciences and its social use is to be developed as intensively and extensively as it ought to be at the threshold of the atomic age. Intelligent co-operation is needed in establishing an adequate research program: voluntary organizations, public agencies and individuals must be brought together in the place of reliance on the isolated efforts of a

few organizations and some philanthropists, and international co-operation in research must be fostered. Since the fateful day of August, 1945, on which the atomic age was ushered in, it has become clear to all but those trying to escape from reality that the development of a better social and economic order depends largely on the international co-operation of the intellectual workers and scientists. One may well paraphrase an old rallying cry by saying, "Scientists of the world, unite!" This is the banner we must hold high in the future.

### MEDICAL EDUCATION

There is need for support of undergraduate and postgraduate medical education. The future physician should be competent in health guidance as well as in the diagnosis and treatment of disease. He should also have an understanding of the socioeconomic relation of his profession and be able to participate in the formulation and operation of health programs.

Reorientation of the curriculums of medical schools along these lines is in process. The development of broad and effective teaching programs requires full-time teaching, and this means additional funds to provide the medical schools with men of high caliber who are ready to make teaching a career.

Not less important is a new policy in regard to the selection of students of medicine. At present, many promising young men and women find it difficult, if not impossible, to study medicine because they lack the money for the long period of education. The available scholarships are few. Moreover, there seem to be medical schools that restrict the number of students from certain groups. This impression was confirmed by recent events in the state of New York. In regard to adequate educational provisions for Negro students, the record is anything but unblemished.

The great upheaval of the war has brought with it a wave of enthusiasm for reinterpretation of democratic concepts. The training program of the armed services, whatever may be said against it, certainly had one excellent feature. It made it possible for qualified young men without resources of their own to study medicine. This is democratization of education, and from this principle there should be no retreat. If the individual is to be given the freest possible play for his talents, a large number of adequate scholarships must be provided for promising young men and women planning to enter the medical profession.

### DEMOCRATIC IDEALS

The task now facing this country is gigantic. It is beyond the power and the financial resources of any individual, any single group or any single state, and requires nation-wide effort for its execution.

In reviewing the facts, repeated reference has been made to the relation of the various problems to democratic ideals. To give this presentation its proper perspective a few remarks may be added on the philosophy underlying the present movement for a national health program.

The Virginia Bill of Rights of 1776 stated that all men have certain inherent rights, namely, "the enjoyment of life and liberty, with the means of acquiring and possessing property and pursuing and obtaining happiness and safety." The Declaration of Independence, enunciating the fundamental democratic tenet that men possess the natural rights of life, liberty and the pursuit of happiness, did not go so far as the Virginia Bill of Rights. By tacit consent, however, the words of the Declaration of Independence have been interpreted as including the right to obtain health service.

With the evolution of democratic thought its individual doctrines, particularly those of equality, freedom and social justice, have assumed new meanings. Abstract objectives are being redefined and clarified in the light of the needs and potentialities of the present civilization. A growing number of statements include in the fundamental human rights the right to medical care. A report made in 1939 by a Senate subcommittee states<sup>9</sup>

The ideals and principles of American democracy call for equality of opportunity. Such equality of opportunity certainly cannot exist unless all groups in the population have access to those health services needed to prevent and cure disease, and to promote vitality and well being.

There is nobody in this country who would object to this statement. The difference of opinion arises when the methods of social action come up for discussion. Some people question the feasibility of over-all planning for health service, talking deridingly of "planomaniacs" or flatly refuse to accept any change in existing patterns. Those holding such opinions should remember Thomas Jefferson's words:

I am not an advocate for frequent changes in laws and constitutions. But laws and institutions must go hand in hand with the progress of the human mind. As that becomes more developed, more enlightened, as new discoveries are made, new truths discovered and manners and opinions change, with the change of circumstances, institutions must advance also to keep pace with the times.

310 Cedar Street

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## OSSEOUS SYPHILIS\*

## Report of a Case

MARK EXLEY M.D.,† AND A W. NEWTON M.D.‡

UNUSUAL and extensive involvement of the osseous system by syphilis occurring thirteen months after the appearance of the secondary skin manifestations is indeed of interest. It is known that wide dissemination of spirochetes through the body tissue occurs within three or four hours after the initial infection. Even though the bone, with its periosteum and blood-forming marrow cavity, contains myriads of spirochetes, skeletal involvement is comparatively rare.

Much has been written by the earliest syphilologists vividly describing the symptoms—the pathognomonic osteopathic pain and bony swelling that occur in skeletal syphilitic involvement. The case reported herein is that of a patient who suffered a spontaneous pathologic fracture.

F. B. (No. 62,490), a 26-year-old man, entered the hospital on December 28, 1942, complaining of progressively increasing pain in the right arm and both thighs of 3 weeks' duration.



FIGURE 1 Two X-Ray Films of Right Upper Arm (December, 1942)

The humerus shows beginning bony destruction and marked periosteal elevation.

patient was unable to understand how he had contracted the disease, since he had never had a penile lesion. Additional interrogation elicited the fact that he had a negative serum reaction approximately 6 months prior to the involvement, when he had had a routine examination while seeking employment.

Physical examination revealed a poorly developed, emaciated pale young man. The head and neck were essentially normal. The heart, lungs and abdomen were normal. There



FIGURE 2 X-Ray Films of Lower Legs (December, 1942)

There is a marked osteitis of the midportions of both tibiae, with moderate periosteal elevation.

was an irregular raised area on the surface of the midportion of the right humerus, which was tender on palpation. Tenderness could be elicited over the entire length of both femurs. There were marked thickening and irregularity and tenderness of the left tibia.

The red-cell count was 3,500,000, the hemoglobin 9.3 gm, and the white-cell count 7300. The Kahn reaction was + + + +, and an Eagle test was positive.

X-ray examination on admission revealed a large area of destruction at the junction of the middle and distal thirds of the right humerus (Fig. 1). There was marked periosteal elevation, with erosion of the bone. A reaction zone was present. The left lower tibia (Fig. 2) showed marked osteitis involving the midportion of the shaft. There was definite erosion of the bones with reaction zones about them. There was moderate periosteal elevation. The femurs (Fig. 3) showed remarkable change. There was tremendous proliferation in the midportions of both bones. Definite erosion was present, and the involved areas were indistinct and had the appearance of ground glass. The clavicles were normal.

The patient absented himself without leave before further studies could be made of the skull and chest and before treatment could be instituted. He re-entered the hospital in January, 1943, but again left on the following day before

and of loss of strength, extreme weakness and general malaise. The past history revealed the usual childhood diseases. There had been no injuries or operations, and venereal disease was denied. The patient developed a rash 13 months previous to admission. His physician told him that he had a "positive blood reaction" and advised him to take treatment. The

\*From the United States Public Health Service, United States Marine Hospital, Norfolk, Virginia.

†Surgeon (R), United States Public Health Service.

‡Passed assistant surgeon (R), United States Public Health Service.

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any further investigation could be performed. He entered the hospital for the third time on July 24, complaining of severe pain through both thighs, the right arm and the forearm, especially at night. He had recently fractured right arm by bumping it against a chair. The arm thereafter became swollen and painful on movement.

Physical examination revealed a poorly nourished, chronically ill man with a marked pallor. He was depressed, uncooperative and unable to walk without aid. The pupils and fundi were normal. The heart and lungs displayed no

mycosis, but it was decided that the bony changes were syphilitic.

Specific treatment was instituted, consisting of bismuth subsalicylate every 5 days and potassium iodide. Mapharsen was given following the bismuth in gradually increasing doses once weekly. A moderately severe Jarisch-Herxheimer reaction was apparent following the first injection. The patient complained of severe pain corresponding to the areas of bone involvement, but this pain disappeared in 24 hours.

After 2 months of therapy, x-ray examination was repeated. The periosteal elevation present in the films of both ulnas on July 30 had disappeared. The bone destruction in the left ulna had persisted, but the reaction zone about the lesion had decreased. The film of the right humerus (Fig 6) showed that the fracture had healed in good position and that the eroded bone was filling in well. The entire process in both femurs (Fig 7) showed evidence of beginning involution. There were marked irregularity and thickening of the distal portion of the left tibia (Fig 8).

After approximately 4 months of treatment the patient again absented himself without leave, and all attempts to contact him for further study have proved futile.

### DISCUSSION

The areas of the skeletal system most frequently involved in osseous syphilis are the cranial bones, the tibia and the shoulder girdle, especially the



FIGURE 7 X-Ray Film of Thighs (September, 1943)  
The lesions in both femurs are beginning to involute following therapy.



FIGURE 8 X-Ray Films of Lower Legs (September, 1943)  
Both tibias show considerable improvement following treatment.

change. The spleen was palpated on deep inspiration. The reflexes were physiologic. The skin was clear. There was no adenopathy. There was extreme tenderness with no associated sense of heat over the middle third of the right humerus. There was definite deformity of the carrying angle. The midportion of the left ulna appeared bowed and tender. Both femurs felt thickened and were moderately tender. The red-cell count was 3,340,000, the hemoglobin 9.4 gm., and the white-cell count 5800, with a normal differential. A Kahn test was + + + +, and an Eagle test was positive. A test for Bence-Jones protein was negative, and the levels of blood calcium, phosphorus and phosphatase were within normal limits. The spinal fluid, including a serologic test, was normal.

X-ray examination of the lungs, heart and great vessels was negative, whereas that of the skull showed numerous circumscribed areas of decalcification in the parietal and frontal bones. The ulnas showed periosteal elevation and bone destruction. The right humerus (Fig 4) exhibited marked extension of the process since the first admission. A fracture was visualized in the midportion. The process in the left tibia had progressed slightly. The femurs (Fig 5) showed extension of the process on the left involving the shaft up to the intertrochanteric region. The periosteum of both femurs demonstrated an onion-skin appearance, which was marked on the right.

The differential diagnosis included tuberculous osteitis, multiple myeloma, osteitis fibrosa cystica, pyogenic osteomyelitis, osteolytic metastatic carcinoma, Hodgkin's disease, leukemia, with its bony infiltration, actinomycosis and blasto-

clavicle toward its medial aspect, but lesions are often observed in the ribs and the sternum.

Histologically, the lesion is usually a periostitis, but there is less tendency toward osteoplastic bone proliferation in early syphilis than during the later stages of the disease. At first, the fundamental process is one of osteolysis, with replacement of granulation tissue. Osteitis, however, is more frequent in early than in late syphilis, and it may assume a



FIGURE 3 X-Ray Film of Thighs (December, 1942)  
Proliferative processes are present in the midportions of both femurs



FIGURE 5 X-Ray Film of Thighs (July, 1943)  
The lesions in the femurs show considerable advance as compared with those present seven months previously



FIGURE 4 X-Ray Films of Upper Arms (July, 1943)  
The right humerus shows a pathologic fracture, which occurred approximately seven months after the patient was first seen. The left humerus is essentially normal.



FIGURE 6 X-Ray Films of Upper Arms (September, 1943)  
The fracture of the right humerus has healed, and after two months of treatment the eroded bone is filling in well.

## CLINICAL NOTE

## GENERALIZED DERMATITIS FROM PEDICULOSIS CAPITIS\*

F RONCHESE, M D T

PROVIDENCE, RHODE ISLAND

IN a recent article, Morris<sup>1</sup> has called attention to pediculosis corporis as an overlooked cause of ulcers of the legs in middle-aged patients. The present paper emphasizes pediculosis capitis as an overlooked cause of a generalized dermatitis.

The usual descriptions of the dermatitis accompanying pediculosis capitis give as its location the scalp and the neighboring areas of the neck. Not infrequently, however, the eczematoid, prurigo-like dermatitis extends far beyond these limits, in some cases it involves the entire cutaneous surface, as in pediculosis corporis. The main difference is that in pediculosis corporis the patient is likely to be elderly, destitute and homeless, and the dermatitis is actually caused by the biting pediculi, followed by scratching. In pediculosis capitis, however, the patient is usually of school age or slightly older, with access to bathing and clothes-changing facilities, and the dermatitis is self-inflicted, resulting from a neurogenic pruritus originating in the skin of the scalp. One may take exception to the neurogenic explanation, however, and argue that the allergen is carried directly from the scalp to the sensitive skin by the patient's nails.

The sensation of itching noted by the examiner of a lousy scalp is a frequent experience, and one can easily imagine the feeling of the host to the pediculi. If the patient has a sensitive skin, he scratches and scrubs his skin furiously. This does not disturb the pediculi, but produces a body dermatitis that fails to respond to calamine or any other lotion and becomes progressively worse.

In most cases the diagnosis of pediculosis capitis produces a shock to the patient and his parents, and one is often told, "Never mind the nits — just take care of the sores." Treatment must be thorough, since so long as a single nit is present, the dermatitis of the scalp, neck and body will continue. As soon as delousing is complete, however, the dermatitis promptly disappears.

A dermatitis of this origin involving the entire body is found only occasionally, but it must be kept in mind, since otherwise the physician's diagnostic ability will be seriously challenged.

During the last few years I have seen several cases in which the correct diagnosis had been missed. One patient was an eighteen-year-old, married

woman, apparently healthy, whose hair was swarming with pediculi (Fig 1). Another was a fourteen-year-old girl who for over a week had been under the care of an experienced pediatrician for an unrecognized, extremely pruriginous dermatosis. She had had some fever, crying spells and anorexia. Examination revealed pediculi on the scalp, and

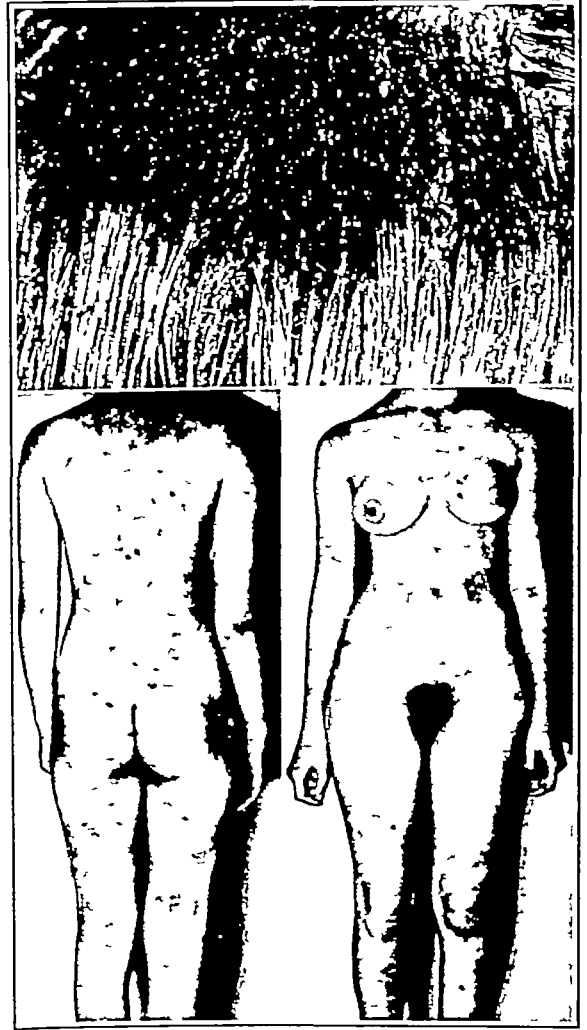


FIGURE 1

*The upper photograph shows the hair covered with nits and swarming with lice. The lower ones show the generalized prurigo-like dermatitis of neurogenic origin. The lice were limited to the scalp and as soon as they and the nits were removed, the dermatitis promptly disappeared.*

the correct diagnoses of pediculosis capitis was easily made. There was a reasonable excuse for failure to detect the presence of pediculi, because the patient had blond hair, in which nits are difficult to identify, especially if they are few in number and are scattered over the scalp.

\*From the Department of Dermatology, Boston University. Instructor in dermatology, Boston University School of Medicine, dermatologist, Massachusetts Memorial Hospitals and Rhode Island Hospital.

diffuse or localized gummatous involvement Sante<sup>1</sup> states that the cortex gradually develops a dense, thickened irregularity and that this is seldom attended by reaction of the periosteum Part of the pathologic and anatomic changes due to syphilis are distinctly and characteristically gummatous There are, however, other changes that are similar to those found in chronic inflammation of the bone produced by other causes, the distinguishing point between the two processes being the comparative mildness of the manifestations of syphilitic involvement

Pathologic fractures are not infrequent, but in most cases they appear to be associated with neurogenic syphilis rather than with syphilitic involvement of the bone In the present case, the cerebrospinal-fluid examination was negative It is not surprising that pathologic fractures are relatively rare when one considers that the usual bony disease process is one of proliferation rather than of destruction This case, however, illustrates coexisting osteogenic and osteolytic processes The fracture described above occurred in an area of destruction

In patients with osseous lesions the initial injection of an arsenical is often followed by an acute exacerbation of pain The pain may last for a period of six to thirty-six hours, but the periosteal reactions rapidly subside This is usually followed by prompt relief of all pain Moore<sup>2</sup> states that if the involvement of the whole bone is present, the subsidence of the painful symptoms may be gradual, requiring a period of days or even weeks The iodides are unquestionably an adjunct in treatment and are indicated in combination with the heavy metals during the course of treatment Thyroid disease, tuberculosis and intolerance to iodides are the only contraindications to their use Clinical improvement is a better criterion for effective treatment than is the serologic response Roentgenologically,

improvement or lack of improvement depends on the type of bony involvement In the proliferative types, little if any change may be noted, even over a period of many years In a small percentage of cases with demonstrable bone destruction, treatment causes deposition of new bone in the diseased areas Persistence of a positive serologic reaction is of no prognostic importance and does not imply an unfavorable prognosis Likewise, a reversal of the serum reaction to negative offers no guarantee against later relapse The physician should not think of effecting a cure but only of arresting progress The patient should be closely followed for twenty-four months

Finally, the ideals to be achieved are as follows The lesions should be healed, the symptoms relieved, relapse prevented, and the progress of the disease arrested

### SUMMARY

An unusual case of osseous syphilis is reported, and certain aspects of the diagnosis and treatment of this disease are briefly discussed

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stages of adolescence will be recognized. These will be referred to as prepubescence, pubescence and postpubescence. The term "pubescence" (or the pubescent period) taken in its literal sense refers to the period of time during which the pubic hair is developing. The various criteria by which these three stages may be recognized clinically will, however, receive attention in various sections of this review.

The adolescent period is one during which profound changes take place in physical, physiologic, mental and emotional development. Since the literature dealing with these changes is voluminous and leads into many diverse fields, it will be necessary to restrict the scope of this report in a number of ways. Attention will be limited to physical growth and the principal physiologic changes of interest in clinical medicine. Much attention will be given to the individual or group variations that are encountered in apparently normal persons, but pathologic processes as they affect growth and gross abnormalities of growth will not be considered. Furthermore, it will not be possible to deal fully with the studies of fundamental genetics, endocrinology and ecology to see what light they shed on the causes for the changes observed with growth and development during adolescence. The endocrine glands will be briefly considered from the viewpoint of their development and functioning during this period. Although the study of the hormonal control of the growth processes is a fascinating one, it would require a separate report. A few articles that throw light on the effects of different environmental forces in modifying the progress of adolescent changes will be considered, since they appear to have significance in relation to health and medical care during this period.

#### LONGITUDINAL STUDIES OF THE GROWTH AND DEVELOPMENT OF NORMAL CHILDREN

Davenport and Boas may be considered to have been pioneers in the movement to arrive at a better understanding of adolescence by repeated observations of adolescents over long periods of time. Davenport<sup>1</sup> established the forms of the average curves for growth in height and weight by this method and demonstrated that a so-called "adolescent spurt of growth" is a characteristic phenomenon. He also clarified the differences between the two sexes in the time and magnitude of this occurrence and emphasized the wide individual variability in these respects.

It is of interest to re-read the paper published by Boas<sup>2</sup> in 1932 in the light of many of the studies published since that time. He based his conclusions on careful repeated measurements, determination of the age of first menstruation in girls and other data obtained for children attending the Horace Mann School in New York City, some of whom were followed during the succeeding college years. In the

article referred to, he reported many findings that have since been substantiated by workers dealing with larger numbers of children, particularly in regard to size and rate of growth in relation to the period of maximum growth and the age at which the menarche occurs. He introduced the question whether his findings did not imply a different tempo of physiologic changes in different persons, a suggestion that has since been clearly demonstrated. Credit will not be repeatedly given to Boas when considering the many aspects of growth and development for which he deserves recognition, because later work offers more adequate reference material, but the article cited should be looked on as a classic in this field.

At the time of the deliberations of the committees of the White House Conference on Child Health and Protection (1929-1931), interest was aroused in adolescence as a neglected and little understood period. The reports of this conference,<sup>3</sup> as well as of one called during this period by the Brush Foundation and Western Reserve University,<sup>4</sup> revealed many gaps in the knowledge regarding this period. Shortly thereafter, with the financial backing of the General Education Board of the Rockefeller Foundation and the support of other foundations as well as of local institutions, a number of research centers were organized with the primary purpose of following children through their entire adolescence. The purpose was usually to study these children from many viewpoints, but with emphasis on comprehensive personal records rather than on mass statistics. These programs are for the most part still under way, and a large number of reports from these centers have already appeared. Collectively, they give a much clearer concept of the normal course of events and the interrelations between them than would otherwise be possible. The studies here reviewed come from many centers, but the following are the principal examples of this movement for organized research into human maturation: the Brush Foundation, Western Reserve University School of Medicine, Cleveland, the Denver Child Research Council, University of Colorado, the Institute of Child Welfare, University of California, the Adolescent Study Unit, School of Medicine and Institute of Human Relations, Yale University, the Harvard Growth Study, Harvard School of Education, the Center for Research in Child Health and Development, Harvard School of Public Health, and the Co-operative Study of School Children, Harvard University.

The reports of these studies have appeared in various journals, but some of these are not regularly seen by physicians, so that the review of the findings of clinical interest in a medical journal may increase their usefulness. The major reports have appeared in monographs published by the Society for Research in Child Development, National Research Council, Washington, D. C., and in *Child*

The gratification of being able to make an immediate diagnosis in a case of this sort is in contrast to the discouragement experienced in cases of almost daily occurrence in which one is faced with a mysterious dermatosis or psoriasis

#### SUMMARY

In pediculosis capitis, besides a dermatitis limited to the scalp and neck, one must keep in mind that

not infrequently a neurogenic pruritus is present. This causes a generalized dermatitis, which is some times difficult to interpret

170 Waterman Street

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## MEDICAL PROGRESS

### NORMAL GROWTH AND DEVELOPMENT DURING ADOLESCENCE\*

HAROLD C. STUART, M.D.†

BOSTON

**A**DOLESCENCE, according to Webster's first definition, is "the state or process of growing up from childhood to manhood or womanhood," and this is the meaning that will be given to the term in this review. Some confusion is apparent in the literature because a second definition by Webster limits adolescence to a much shorter terminal phase of the developmental period — that is, "the period of life between puberty and manhood."

As examples of the confusion caused by this difference of interpretation, one author refers to the "pubescent period" in girls as that preceding the menarche and the "adolescent period" as that following this event, but in another connection he refers to adolescence as "a period of rapid growth." The term "adolescent spurt of growth" so frequently used in the literature is a misnomer if adolescence begins at puberty, for it is then a preadolescent phenomenon. Another author gives the ages of onset of adolescence in a group of normal children under close observation as 7 3/12 to 13 6/12 years for girls and 10 9/12 to 13 11/12 years for boys. These ages indicate that adolescence is considered by him to include the pubescent period or to begin before puberty, in the sense in which this term is ordinarily employed. According to Webster, puberty is "the state or quality of being first capable of begetting or bearing offspring, which is marked by the maturing of the reproductive organs with the onset of menstruation in the female and the development of the secondary sex characters in both sexes, the period at which sexual maturity is reached." In the light of present knowledge this definition is not tenable, since the onset of menstruation and the attainment of the ability to bear children are

far from identical. The term "puberty" is some times used in the literature when referring to girls as synonymous with the menarche or the time of occurrence of the first menstrual period. It is, however, oftener employed as referring to the whole period during which the secondary sex characters are developing, leading up to the menarche. It is of necessity used with a rather indefinite connotation when referring to boys, but in general it indicates the period during which the secondary sex characters are developing. To avoid confusion, the term "puberty" will not be used in this review except when direct reference is made to statements in the literature.

It is difficult to select suitable criteria for the beginning and end of adolescence, but as this review progresses it will become evident that according to the first definition, which is the one accepted here, it covers a long portion, roughly the second half, of the period of development. Adolescence begins and ends much earlier in girls than in boys and in some persons than in others, and the early and late changes indicative of the period occur gradually and are usually not readily observed. As the early indications of sexual differentiation are considered it will become evident that by certain criteria, as, for example, an appreciably increased excretion of sex hormones, an earlier age of onset can be assigned than would be possible if one were guided by the first appearance of clinical signs of sex differentiation. Adolescence ends when functional reproductive capacity is fully established and the child has thus become an adult. Again, the time of arrival at this state is not easily recognized, and it probably differs widely between persons, but the evidence that will be reviewed suggests that it is near to the ages at which boys and girls are usually considered to have reached manhood or womanhood. For purposes of presentation in this review, three

\*From the Department of Maternal and Child Health, Harvard School of Public Health, the Department of Pediatrics, Harvard Medical School and the Children's and Infants' hospitals, Boston.

†Associate professor of child health, Harvard University, head of Department of Maternal and Child Health, Harvard School of Public Health, visiting physician, Children's and Infants' hospitals.



stages of adolescence will be recognized. These will be referred to as prepubescence, pubescence and postpubescence. The term "pubescence" (or the pubescent period) taken in its literal sense refers to the period of time during which the pubic hair is developing. The various criteria by which these three stages may be recognized clinically will, however, receive attention in various sections of this review.

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*Development*, the journal of this society. These publications will be useful to physicians interested in adolescents.

Out of all these extensive studies, reinforced by many special or restricted ones, the substance of only a few can be considered here. Several previous reviews may be consulted by those who wish a more complete bibliography, especially those by Greulich and his associates<sup>5</sup> and by Shuttleworth,<sup>6</sup> both published in 1938, and that by Jones and a committee of the National Society for the Study of Education,<sup>7</sup> published in 1944.

### PHYSICAL GROWTH

In studying the growth of children, curves based on averages for each age have some value in showing general trends, but they must be interpreted guardedly, for they tend to mask characteristic differences among various types of persons. This is particularly important in considering growth during the adolescent years, when such wide differences in progress are encountered between those who mature early and those who mature late. A few general features of growth will be deduced from the composite curves before individual and group differences are discussed.

The following brief statement regarding the rate of growth in height and weight by year of age and by sex is based primarily on a recent report by Simmons.<sup>8</sup> This report gives average figures from repeated measurements taken at the Brush Foundation throughout the adolescent years in a large number of children. The averages obtained from this source may be somewhat advanced for the United States as a whole, since the children enrolled did not represent a true sample of the population but a group representing rather better than average socioeconomic levels. These averages are, however, in close agreement with those obtained for girls by Dearborn and Rothney,<sup>9</sup> from the Harvard Growth Study, by the Ministry of Health of Canada on Toronto school children<sup>10</sup> and from other extensive sources in the United States, some of which are referred to later in this report. The curves produced by the yearly increments in height and weight obtained by Simmons are quite different from some obtained by workers in other countries or in earlier years—for example, those based on German data reported by Pfuhl in 1928, as presented by Greulich.<sup>11</sup> The possible explanations for these differences are briefly discussed below.

Considering only average occurrences, the rate of growth in height—that is, the increment year by year—is continually diminishing from birth to maturity except for a short period that is referred to as the adolescent spurt of growth. The rate of this decrease is rapid during the first two years but diminishes year by year during the preschool period. During the early school years it becomes so slow that the curve of increments appears almost flat.

According to Simmons, girls gain in height at an accelerating rate from nine to twelve years, whereas boys do so from eleven to fourteen years. This results in the fact that girls are taller than boys between eleven and thirteen years. From thirteen years in girls and fifteen years in boys the rate of growth in height decelerates rapidly, and after about three years it ceases. According to these yearly averages, the twelfth year in girls and the fourteenth year in boys appear to be those of maximum growth. As will be seen in connection with more detailed studies of different groups of children, maximum growth actually takes place most frequently at some time during the thirteenth year in girls and the fifteenth in boys, but the inflection in the curves takes place during these years also. It is for this reason that the total gains average less during these than the preceding one for each sex. During the three years of upward trend different groups of children are taking shorter, sharper single spurts of growth at different ages, for reasons which will be discussed, so that the composite curve becomes flattened and broadened. Thus, the child actually grows at a much more rapid pace than the composite curve suggests, but for a shorter period of time.

The average increments for weight by years show a somewhat different picture. Following the initial infantile spurt of growth, deceleration takes place more rapidly for weight than for height, and the increment each year remains about the same between two and five years, a period during which it is smaller than at any other time before maturity. From five years onward there is a slight but progressive increase in gain each year.\* This acceleration of gain in weight becomes much more rapid at the time when accelerating growth in height begins, and it terminates at approximately the same time as does that in height, although it tends to be spread over a somewhat longer period. The curves produced by the increments for height and weight for both sexes are reproduced from Simmons's monograph in Figures 1 and 2.

The pattern of linear growth as exemplified in the curves for height is followed in the main by the principal body dimensions and even by the small bones of the hand, as shown by Shuttleworth<sup>12</sup> from measurements taken on roentgenograms. Yet growth is not uniform in the percentage of mature size added in the different dimensions in any given year, or even in the exact age at which maximum growth occurs. Changes in the form and proportions of the body are constantly occurring. In con-

\* This gradual rise in the increments for weight from five to ten or twelve years leading up to the major adolescent acceleration has been considered by some investigators to be part of this whole cycle and an early sign that the changes that lead to pubescence are already operating. Linear growth is actually diminishing during this period, however, and the gain in weight may be associated with other factors. In fact, measurements of large numbers of children in other countries or under special conditions fail to reveal a rise during much of this period. Hence, this early rise as generally shown in the United States may be a manifestation of this country's particular dietary customs and socioeconomic conditions.

formity with the law of cephalocordal progression of relative growth increase, whereas during early adolescence the head has practically completed its enlargement, the lower segment is growing rapidly. Growth in the legs slows down and ceases somewhat before that in the trunk, however, so that the sitting height-stature index, which becomes smaller each year

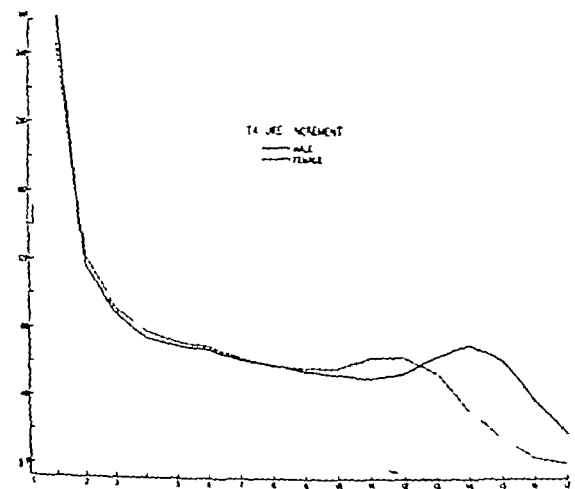


FIGURE 1 Stature Increment according to Chronological Age (reproduced from Simmons,<sup>8</sup> by permission of the author)

during early adolescence, reaches a plateau before puberty and is slightly reversed after it. With the use of hip ratios to reveal relative breadth-length growth, it has been found that from about twelve years onward girls become relatively broad-hipped whereas boys maintain a constant ratio. On the other hand, when hip width and shoulder width are

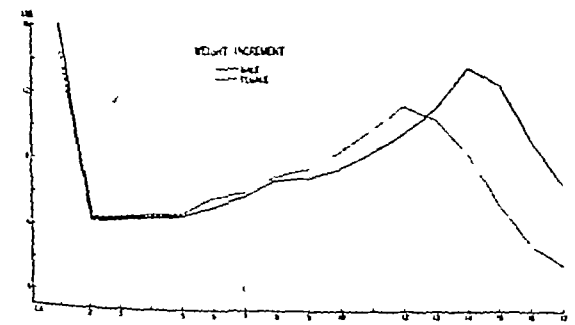


FIGURE 2 Weight Increment according to Chronological Age (reproduced from Simmons,<sup>8</sup> by permission of the author)

compared, boys are found to progress more rapidly in shoulder breadth, whereas girls progress more rapidly in pelvic breadth. Bayley<sup>12</sup> has shown that girls exceed boys in pelvic breadths at all ages from eleven to sixteen years, but thereafter the two sexes are nearly alike in this measurement, owing to the generally larger size of boys.\* In biacromial

shoulder breadth, girls exceed boys from eleven to fourteen years owing to their general advancement but thereafter boys greatly exceed in this measurement owing both to more rapid general growth and to greater broadening out in this area. These and other differences in rates of growth during adolescence lead to the characteristic differences between men and women in average size, build and contour.

Meredith<sup>14</sup> for boys and Boynton<sup>15</sup> for girls give means for eighteen body measurements for each age up to eighteen years, as well as increments for each of these at the successive age intervals. In subsequent publications these authors<sup>16, 17</sup> give further anthropometric norms, and Gray and Ayres<sup>18</sup> give norms for some of these measurements based on studies of private-school children. Although many other tables of norms based on studies of large groups of children have been published and are useful as standards, the references cited are as complete and representative as any available for clinical purposes. In Table 1 a few of the segmental and sex differences

TABLE 1 Segmental and Sex Differences according to Year of Maximum Growth

MEASUREMENT	YEAR OF MAXIMUM GROWTH	
	BOYS	GIRLS
Weight	15	12
Height	14	12
Sitting height	15	12
Shoulder breadth (biacromial)	14	12
Pelvic breadth (bi-iliac)	—	13
Hip breadth (bitrochanteric)	14	—
Thoracic circumference	14	11

that emerge during adolescence are revealed by the ages at which maximum growth occurs in some of the principal measurements for each sex, as given by Meredith and Boynton.

INDIVIDUAL VARIATIONS IN GROWTH

Davenport,<sup>1</sup> in the studies previously referred to, called attention to the marked differences between children of the same age — in the age at which the adolescent acceleration in growth begins and ends and in the magnitude of this spurt of growth. Many studies dealing with these differences have appeared since Davenport's description was published. Shuttleworth<sup>19</sup> has shown that when the yearly increments of gain in height for different groups of girls selected on the basis of their ages at the time of maximum growth are charted with the years of maximum growth superimposed, the several curves fit remarkably well but differ in their magnitudes. These studies will be further discussed in considering the relation of this cycle of growth to the menarche. The same applies for the curves of weight increments for boys and for those of weight and other dimensions for both sexes. The point of importance to be derived from all these studies is that

\*The development of the pelvis in girls is described in connection with the secondary sex character.

children pass through the adolescent phase of accelerated growth at widely different chronological ages, but that in all aspects of growth they follow much the same sequence or pattern for any particular measurement regardless of when the adolescent phase is initiated. Thus, when chronological age is ignored and age of either initial growth acceleration or maximum growth is substituted, there is far greater uniformity between children. Certain differences have, however, been recognized between children taking this growth very early and those taking it very late. Children having early occurrence of maximum growth tend to differ from those having late occurrence in the following ways: the maximum increment is greater in amount, the whole cycle is completed in a shorter time, the children are larger before maximum growth but are likely to be more alike or even shorter at the end because growth is completed more quickly, and maximal growth occurs early rather typically in broad-hipped persons and those with relatively short legs — that is, in those with a feminine configuration.

The actual variability in age of maximum growth is suggested by Shuttleworth's analysis of its occurrence among 174 girls. In 6 cases it occurred between  $10\frac{1}{4}$  and  $10\frac{3}{4}$  years, and the numbers for each successive six-month age interval were respectively 13, 26, 34, 37, 28, 18, 7 and 5, the last falling between  $14\frac{1}{4}$  and  $14\frac{3}{4}$  years. In 99 of 174 girls, or more than half, it occurred between  $11\frac{3}{4}$  and  $13\frac{3}{4}$  years. For boys the distribution was approximately the same but occurred two years later. The stimulus to be advanced or retarded in growth is a general one and affects all dimensions. One may therefore use age of maximum growth, preferably in height, as an indication of the characteristics of a given child in respect to his speed or advancement of growth. In later sections this variability in the timing of growth changes will be related to variability in maturation in other respects.

For correlation with other indices of adolescent development, the significant points about physical growth may be summarized as follows. As shown by average occurrences in groups of healthy children in the United States, the change from a decelerating rate of growth in height to an accelerating one, which marks the beginning of the adolescent spurt, occurs during the tenth year in girls and during the thirteenth year in boys. The change from an accelerating to a decelerating rate occurs in the thirteenth year in girls and in the fifteenth year in boys. A change from a slow to a more rapidly accelerating gain in weight occurs at about the same time as the first inflection in height increments, and a change from an accelerating to a decelerating rate occurs at approximately the same time as does that for gain in height. Second, the change from a decelerating to an accelerating rate of growth in

height — as in most linear dimensions — represents a characteristic stage in adolescent development, and this can usually be recognized when subjects are measured at regular intervals. It is more readily recognized and is more certainly attributable to a stage of development than is the initial stage of adolescent acceleration in gain in weight. The latter is likelier to be a gradual change from slight acceleration to greater increments and is more irregular. Third, the period during which maximum growth takes place is much more easily recognized than is the beginning of acceleration, because the increase in the rate of gain is usually much greater. One cannot be sure that the maximum has been attained until measures of the first phase of deceleration are at hand, but a study of the amounts of gain period by period makes it possible to conclude that the maximum has probably been reached or that the point of inflection in the curve is about to take place. Other physical characteristics, usually associated with maximum growth, described below, help to identify this period. Lastly, the time interval between onset and termination of adolescent acceleration in growth in height averages three years but is usually much shorter for the individual. When children are divided into groups on the basis of the age at which they attain maximum growth, the duration of the period of acceleration for the separate groups averages about two years. Those maturing early may complete this phase in about a year, and late or slower maturing persons usually take considerably longer. The duration of the accelerating period is somewhat longer for measurements of breadth. On the average, the duration of the period of rapid gain in weight is greater than that of growth in height, owing to the influence of acceleration in other measurements that precede or follow that of height.

#### GROWTH OF PRINCIPAL TISSUES

The adolescent spurt of growth has a far greater proportional magnitude for weight than for height. This is due in part to a tendency to accumulate larger quantities of fat in the subcutaneous tissue during adolescence, a trend that is more pronounced in girls than in boys. McCloy<sup>20</sup> used subcutaneous tissue calipers for measuring folds of skin and subcutaneous tissue in conjunction with certain circumferences as aids in interpreting body weight. He gives values for these tissues in various parts of the body by age and by sex, the sex differences in this attribute are strikingly shown in his tables. Stuart and Sobel<sup>21</sup> in studies of tissue breadths in the calf, as visualized in x-ray films, have shown this same sex difference at all ages up to thirteen years, the latest age for which measurements were available. At thirteen years the thickness of these tissues is increasing at an accelerating rate, indicative of the tendency to accumulate fat during

pubescence. This study shows particularly how enormously persons of the same age differ in this attribute, but demonstrates that any one child tends to have much or little subcutaneous tissue quite consistently at all ages. Fat children, however, tend to be increasingly fat during infancy and in the period of pubescence and less strikingly so during the intervening years. The obesity of adolescence can be looked on in most cases as an exaggeration of a normal tendency, possibly complicated by the particular emotional factors, food habits or lack of activity usual at this time.

The large increase in weight associated with the rapid growth of pubescence is also accounted for in large measure by broadening of the skeleton and increased massiveness of individual bones, which is shown by the incremental curves for most transverse and circumferential measurements of parts where bones are prominent. This increased stockiness of bones becomes much more marked in boys than girls during the late adolescent years, as exemplified by the differences in the growth of the jaws and facial bones in the two sexes. The muscles are also growing rapidly at this time, and this is again more marked in boys than in girls. This accounts for a considerable part of the gain in weight, although members of both sexes differ greatly in this respect. Muscle development is such an important part of normal adolescent progress that it deserves attention from the clinician conducting health examinations during these years. Muscle size, which is being considered here, is only one factor in muscle strength and functional fitness, but it should be assessed in its own right and in relation to the interpretation of body weight.

The measurements of breadths and circumferences for which tables are given by Meredith and Boynton and by McCloy in publications already cited serve particularly to recognize differences in the stockiness of bones and the size of muscles.

The rate of urinary excretion of creatinine may be taken as a measure of muscle weight, hence the curve of increase with age in this excretion can be used as a measure of muscle growth. Talbot<sup>22</sup> has estimated that 1 gm. of urinary creatinine excreted in twenty-four hours represents 17.8 kg. of muscle weight. In a study of children in a private school, total twenty-four-hour urinary excretions of creatinine were measured in girls and boys at each age from six through fifteen years.<sup>23</sup> The numbers of children studied were small at all ages, but especially so at six and fifteen years. The variability for each sex at each age was great, but the trend of the means was progressively upward and at an accelerating rate at the older ages. At all ages from six to twelve, inclusive, the boys excreted 10 to 20 per cent more creatinine than did the girls, and at fifteen years the few boys studied showed great individual difference. A few had extremely high

values. The increases by year in both sexes were highly irregular owing to the small samples, but for both sexes combined they were relatively small up to nine years of age, then larger to thirteen years and much larger between thirteen and fifteen years. Although this trend must be confirmed by the study of more children, it is what might be expected from body measurements. At the age of fifteen and thereafter the differences between boys and girls would certainly be expected to increase appreciably. The implication is that maximum growth in muscle mass is a late occurrence, following that of maximum growth in height but contributing to maximum growth in weight.

Dimock<sup>24</sup> has studied the development in boys of physical strength and endurance and in motor abilities, using the Rogers test for physical strength or capacity and the Brace test for motor ability or co-ordination. He finds that strength virtually doubles between twelve and sixteen years, but that the peak of increase takes place after the maximum rate of growth in height and weight and during the years of postpubescence. The tests of motor ability or co-ordination showed continuous moderate improvement, but this improvement was more rapid in the prepubescent and postpubescent periods than during the period just preceding that of maximum growth. Dimock's findings did not confirm the widely accepted view that a substantial loss of motor control and resulting awkwardness are associated with the period of rapid growth.

In 1940, Espenschade<sup>25</sup> reported the results of motor-performance tests applied periodically to a group of adolescent children being followed at the Institute of Child Welfare, University of California. Because of the extensive observations being made on these children, it was possible to study the relation between motor performance and both physical growth and the evidences of maturity. Six tests of motor performance were used that had been found to be sufficiently reliable, valid and consistent for the purpose of giving evidence concerning co-ordination, strength, speed and accuracy. The mean performance of boys in all tests increased steadily and markedly at each age up to seventeen years, whereas girls failed to improve after fourteen years and in some cases showed a decline thereafter. There were marked individual differences in all tests and in both sexes, but boys on the average surpassed girls in all tests, and this difference increased with age.

This field of study has recently been greatly stimulated by a national realization that an unnecessarily large proportion of American youths are handicapped by faulty development or physical defects at the time when they must begin to assume the responsibilities of adult life. Anyone who has devoted much time to the study of adolescents is familiar with the inactive and generally poorly adjusted youth who eats unwisely and excessively,

takes little exercise and in consequence becomes fat and flabby and performs poorly in tests of physical fitness. It is a pertinent question whether lack of regular physical activity and effort during the years in which muscles naturally enlarge and strengthen rapidly may not lead to permanent underdevelopment in this respect. Adequate but controlled use appears to stimulate muscle development and is probably most effective when muscles are developing most actively. Possibly the likes and habits of girls during these years, since girls are less athletic than boys, lead in part to late sex differences in muscularity. It does appear that psychologic problems in adolescence may have much to do with the rounding out of physical development in this respect and that they deserve attention. Shuttleworth has pointed out that, since the individual adolescent usually passes through the period of rapid growth in about two years, with one period of extremely intensive growth, and not in the less intense and more prolonged manner suggested by the average curves, force is added to the argument for greater attention to food and other needs during this period.

(To be continued)

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32201

#### PRESENTATION OF CASE

A sixty-two-year-old Italian-born paint and lacquer sprayer entered the hospital because of abdominal pain.

Two months before admission an ache developed in the right upper quadrant of the abdomen, which was constant and not affected by food, exertion, position or respiration. It became progressively worse, and after a month he was incapacitated by it. Three weeks before admission there was radiation to the right shoulder and right flank. During the illness he maintained a good appetite but lost 10 pounds. There were no gastrointestinal symptoms or changes in bowel habits.

For many years he had had a productive cough, worse in the morning. The sputum was usually dirty brown. There had been no blood streaking.

Physical examination revealed a firm mass occupying the epigastrium. The right border of the mass was nodular, but the left border was round. The liver was not felt separately from the mass, nor was the spleen palpable. The prostate was one and a half times its normal size, slightly tender, soft and symmetrical. There was slight clubbing of the fingers. Except for a soft apical systolic murmur the rest of the findings were normal.

The temperature was 100°F, the pulse 102, and the respirations 24. The blood pressure was 142 systolic, 90 diastolic.

The red-cell count was 3,760,000, with 13.5 gm of hemoglobin. The white-cell count was 10,200, with 78 per cent neutrophils. The urine was normal except for bile in one of three specimens. The stool gave a +++ guaiac reaction. The prothrombin time was 25 seconds (normal, 19 to 22 seconds). In the x-ray film, the right dome of the diaphragm appeared elevated and showed a localized shallow lump in its anterior portion. Each lower lobe of the lungs had a small area of atelectasis. At the right of the lower portion of the trachea and in the right tracheobronchial angle there were two oval masses. A small irregular area of increased density was seen in the third right interspace, and a smaller rounded one in

the left fourth interspace. There was still another nodule beneath the left dome of the diaphragm. In the gastrointestinal series curling of the lower end of the esophagus was described. In addition there were defects said to be consistent with varices, as well as a small hiatus hernia. The second portion of the duodenum seemed to be pressed on by a mass, but this finding was questionable. The colon was normal.

Eight days after admission the patient vomited about 400 cc of dark, reddish-black liquid, which gave a ++++ guaiac test. The stools passed after that day were tarry. Within the next two days the hemoglobin dropped to 9 gm, despite transfusions. There was no other hematemesis. He died on the eleventh day, after a fifteen-minute period during which he was unresponsive.

#### DIFFERENTIAL DIAGNOSIS

DR JAMES H TOWNSEND Dr Lingley, will you demonstrate these interesting x-ray findings?

DR JAMES R LINGLEY The film of the chest shows two sharply defined masses in the right paratracheal region projecting into the right upper lung field. There is also an area of density in the right third interspace, and a nodule in the left fourth interspace. The diaphragm is distinctly elevated on the right, and in the lateral view the elevation is found to be anterior. The elevation is more sharply limited and more convex than what one usually sees when it is due to a weak leaf of the diaphragm. It suggests a mass in the liver. This film of the lower esophagus shows curling—a series of rounded bulges of the barium-filled lumen. Fluoroscopically these were inconstant, they came and went and were of no clinical significance. Another film of the lower esophagus shows an irregularity of the mucosa that is indicative of varices. I cannot be sure that they are present. The appearance is suggestive but not characteristic.

DR TOWNSEND Do the films give any idea of the size of the liver or of the shape of the lower border?

DR LINGLEY The liver presses the hepatic flexure downward and extends to the notch of the crest of the ilium.

DR TOWNSEND Do they give any indication of an enlarged spleen?

DR LINGLEY The spleen is probably normal in size, but it is not distinct.

DR TOWNSEND There is also a nodule beneath the left dome of the diaphragm. Is that not an unusual place?

DR LINGLEY I cannot see that nodule.

Here are the films of the stomach, and I should like to point out one thing not mentioned in the record. There is a defect on the lesser curvature at this point, and it is important to decide whether it is due to pressure from the left lobe of the liver or to an intrinsic lesion of the gastric wall. From this one film and without fluoroscopy I am inclined to

think that it was an intrinsic lesion of the stomach I do not want to lead you astray, however, and all things being considered, we should probably believe the fluoroscopist, who found nothing wrong with the stomach

DR TOWNSEND To summarize the significant features of this case, this was a sixty-two-year-old Italian who had an interesting occupation in that he used lacquer and presumably various kinds of chemicals and may possibly have encountered something in that occupation that damaged the liver. He had had symptoms for only two months, and the presenting symptom was pain in the right upper quadrant radiating to the shoulder, which suggests something in the diaphragm. In confirmation of this is a lesion shown by x-ray, which apparently involves the capsule of the liver and the diaphragm. He had had a chronic cough with brownish sputum but never any blood. Shortly before death there was a massive hemorrhage from the gastrointestinal tract. The outstanding physical finding is the large nodular liver. We have laboratory evidence that is mainly negative, except that he had a mild degree of normochromic anemia at the time of entry and was showing blood in the stools even at that time. He also had a prolonged prothrombin time, on which I shall comment later.

The x-ray studies give definite evidence of nodules scattered in the chest, below the diaphragm and in the liver. I think that we must assume that there were at least two nodules of considerable size in the liver, one of which projected into the dome of the diaphragm and the other into the epigastrium. It is difficult to offer any explanation of this patient's picture except one on the basis of widespread malignant neoplastic disease, which involved the chest as well as the liver.

What was the origin of this malignant disease? Was it primary or secondary in the liver? What was the probable point at which it arose? I should like to approach the problem from two angles—first, the probable causes of nodules in the liver, and second, the usual causes of massive hemorrhage in the gastrointestinal tract. I shall try to find a reasonable common denominator. I should like to say now that, if this was metastatic cancer in the liver, it would be unusual for lesions of recent origin to produce certain changes that were present in this case. I am going to assume that there were esophageal varices. It would be unusual for metastatic cancer alone to cause enough disturbance in the portal circulation to produce esophageal varices. By the same token it would be rather unusual for a few nodules in the liver to cause enough disturbance of the liver function to produce an increase in the prothrombin time. It would be interesting to know whether this patient showed other evidence of cirrhosis, because metastatic cancer does not usually produce severe damage of the liver parenchyma itself unless it is extremely extensive. Among the

causes of nodules of this sort, however, the most frequent is metastatic malignancy. One must also consider the possibility of a primary malignancy in the liver, which may have arisen from a pre-existing hepatic disease, such as portal cirrhosis. One must also consider other types of liver disease, such as a long-existing hepatitis, originally acute yellow atrophy, with subsequent regeneration, which sometimes takes the form of nodules that can definitely be felt. This possibility is suggested only by the fact that in his occupation he had dealt with various chemicals. One should also consider echinococcus cyst, but I see nothing in this case to suggest that diagnosis. Syphilis can also produce a nodular liver. I do not know what the serologic tests showed in this case, but syphilis would not explain the nodules in the chest, and I shall rule out that diagnosis.

If we look at the problem from the point of view of the more probable causes of massive fatal hemorrhage in the gastrointestinal tract, we should consider such causes as ulcerating malignant neoplasms of the stomach, the duodenum and the pancreas, as well as peptic ulcer, which can produce fatal hemorrhage and can also coexist with cirrhosis of the liver. We should also consider esophageal varices, which are perhaps the most frequent cause of such massive hemorrhage as this patient appears to have had. Also such a thing as a ruptured aneurysm should be considered, but I do not believe that we have enough evidence in this case to suggest that as a possibility. One should also consider a general bleeding tendency, such as that which occurs in the terminal stages of many chronic constitutional diseases. We have no evidence of that, except the increased prothrombin time. There is no evidence of increased bleeding or clotting time.

From the data at hand it is impossible for me to say, at least with any assurance, what was the primary source of this malignant tumor and whether the lesions in the liver were primary or secondary. If they were secondary, such nodules as these usually come from below the diaphragm—from the stomach, duodenum, pancreas or colon or possibly from the prostate. In this case the patient had an enlarged prostate, but it is not described as nodular or stony hard and nothing is said about it to suggest that it was cancerous. Such nodules can also come from primary lesions in the chest. Indeed, in the last case that I discussed here before the war, there was a large nodular liver, quite similar to this, with two nodules in the lungs, it proved to be a primary carcinoma of the lung, which had been asymptomatic.

Arguing from the fact that this patient appeared to have more liver disease than one would expect from a few nodules, from the presence of esophageal varices, which I believe ruptured and resulted in death and from the presence of a prolonged prothrombin time, I am going to venture an opinion



that this man had liver disease of longer duration than the few months that this malignant disease had existed. My first choice for diagnosis, therefore, is a primary tumor of the liver arising on a pre-existing cirrhosis. I do not believe that that can be backed up clinically, that is, by positive proof during life. As a second choice, I choose metastatic cancer of the liver and lungs, most probably primary in the abdominal cavity, such as in the upper silent portion of the stomach, where it is difficult to demonstrate ulcerating lesions but possibly from the lung. As I have said before, it is impossible to be certain about the point of origin of these malignant tumors.

A PHYSICIAN. There is no mention whether the mass did or did not move with respiration. If we could assume that it did move with the liver it would make a great deal of difference.

DR DONALD S. KING. Dr Townsend remembers a case in which the tumor was primary above the diaphragm with metastases below. The one that I had a few years ago was the other way around — primary in the stomach with metastases to the nodes about the lung roots.

How often does a tumor of the stomach metastasize to the liver?

DR TRACY B. MALLORY. It is quite characteristic. Betting on the wards favored primary cancer in the stomach, with secondary nodules in the liver.

DR CHARLES L. SHORT. If we assume that there was cirrhosis, does that make metastatic cancer less likely? According to statements made in various reports, metastases to a cirrhotic liver are relatively rare.

DR WILLIAM CLARK. In an autopsy done several months ago there was primary cancer of the lung with metastases to a cirrhotic liver.

#### CLINICAL DIAGNOSIS

Carcinoma of stomach, with metastases to liver and lungs

#### DR TOWNSEND'S DIAGNOSIS

Malignant tumor, primary in liver, arising from pre-existing cirrhosis with generalized metastases

#### ANATOMICAL DIAGNOSES

Hepatoma, with metastases to lungs, pincneas, kidneys and mediastinal and retroperitoneal lymph nodes

Cirrhosis of liver

Esophageal varices

Hydrothorax, bilateral

#### PATHOLOGICAL DISCUSSION

DR MALLORY. The autopsy on this patient showed a greatly enlarged liver with large and small tumor nodules jutting out all over the surface. Between the various tumor nodules, however, a few small areas of liver tissue could still be recognized, and

these areas were definitely cirrhotic. Besides the tumor in the liver, the pancreas was found completely replaced by tumor and there were metastases in the lungs. The presence of invasive neoplasm in the pancreas raised doubt at the time of autopsy concerning the nature of the tumor, but there was one point that I think is strong evidence in favor of a hepatoma when one examined the liver from the posterior surface and looked at the hepatic vein, a tumor thrombus was seen to project from the mouth of the vein into the vena cava, and on examination of the rest of the liver all the hepatic veins were found to be filled with tumor thrombi. There are only two tumors that more or less regularly grow into veins in the form of gross thrombi. Hypermephroma is one of them, as you know, this frequently fills the renal vein and later the vena cava. Hepatoma is the other, indeed, it is not infrequent for a hepatoma to show growth up the hepatic vein into the vena cava and sometimes directly into the right auricle of the heart, which may become completely filled with tumor. On this basis I thought at the time of autopsy that the liver was the probable primary source of the tumor. Microscopically the sections do not help us a great deal further. They are consistent with a hepatoma but not particularly characteristic of it. The tumor was certainly undifferentiated, so that a positive histologic diagnosis is scarcely possible. To my eye it does look considerably more like a liver-cell tumor than a pancreatic tumor, and I think that the gross anatomic appearance and the massive venous invasion are enough to substantiate the diagnosis of hepatoma based on a pre-existing cirrhosis.

The terminal episode was almost certainly, as suggested, a rupture of an esophageal varix, since the stomach was filled with clotted blood. We were unsuccessful in demonstrating the point of rupture.

DR TOWNSEND. I should like to ask whether these varices can rapidly develop secondary to malignant disease or whether they take time, years, to develop?

DR MALLORY. On occasion we have seen esophageal varices for which we could determine no cause.

DR TOWNSEND. But is it not true that you usually do not see them associated with a liver full of metastatic cancer?

DR MALLORY. Almost never.

#### CASE 32202

#### PRESENTATION OF CASE

*First admission.* A thirty-year-old housewife entered the hospital because of leukorrhea and metrorrhagia of three months' duration.

The patient had had one child, a normal infant born eighteen months before admission after a long, difficult labor. On physical examination there was tenderness in both lower quadrants just above the

think that it was an intrinsic lesion of the stomach I do not want to lead you astray, however, and all things being considered, we should probably believe the fluoroscopist, who found nothing wrong with the stomach

DR TOWNSEND To summarize the significant features of this case, this was a sixty-two-year-old Italian who had an interesting occupation in that he used lacquer and presumably various kinds of chemicals and may possibly have encountered something in that occupation that damaged the liver. He had had symptoms for only two months, and the presenting symptom was pain in the right upper quadrant radiating to the shoulder, which suggests something in the diaphragm. In confirmation of this is a lesion shown by x-ray, which apparently involves the capsule of the liver and the diaphragm. He had had a chronic cough with brownish sputum but never any blood. Shortly before death there was a massive hemorrhage from the gastrointestinal tract. The outstanding physical finding is the large nodular liver. We have laboratory evidence that is mainly negative, except that he had a mild degree of normochromic anemia at the time of entry and was showing blood in the stools even at that time. He also had a prolonged prothrombin time, on which I shall comment later.

The x-ray studies give definite evidence of nodules scattered in the chest, below the diaphragm and in the liver. I think that we must assume that there were at least two nodules of considerable size in the liver, one of which projected into the dome of the diaphragm and the other into the epigastrium. It is difficult to offer any explanation of this patient's picture except one on the basis of widespread malignant neoplastic disease, which involved the chest as well as the liver.

What was the origin of this malignant disease? Was it primary or secondary in the liver? What was the probable point at which it arose? I should like to approach the problem from two angles — first, the probable causes of nodules in the liver, and second, the usual causes of massive hemorrhage in the gastrointestinal tract. I shall try to find a reasonable common denominator. I should like to say now that, if this was metastatic cancer in the liver, it would be unusual for lesions of recent origin to produce certain changes that were present in this case. I am going to assume that there were esophageal varices. It would be unusual for metastatic cancer alone to cause enough disturbance in the portal circulation to produce esophageal varices. By the same token it would be rather unusual for a few nodules in the liver to cause enough disturbance of the liver function to produce an increase in the prothrombin time. It would be interesting to know whether this patient showed other evidence of cirrhosis, because metastatic cancer does not usually produce severe damage of the liver parenchyma itself unless it is extremely extensive. Among the

causes of nodules of this sort, however, the most frequent is metastatic malignancy. One must also consider the possibility of a primary malignancy in the liver, which may have arisen from a pre-existing hepatic disease, such as portal cirrhosis. One must also consider other types of liver disease, such as a long-existing hepatitis, originally acute yellow atrophy, with subsequent regeneration, which some times takes the form of nodules that can definitely be felt. This possibility is suggested only by the fact that in his occupation he had dealt with various chemicals. One should also consider echinococcus cyst, but I see nothing in this case to suggest that diagnosis. Syphilis can also produce a nodular liver. I do not know what the serologic tests showed in this case, but syphilis would not explain the nodules in the chest, and I shall rule out that diagnosis.

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that this man had liver disease of longer duration than the few months that this malignant disease had existed. My first choice for diagnosis, therefore, is a primary tumor of the liver arising on a pre-existing cirrhosis. I do not believe that that can be backed up clinically, that is, by positive proof during life. As a second choice, I choose metastatic cancer of the liver and lungs, most probably primary in the abdominal cavity, such as in the upper silent portion of the stomach, where it is difficult to demonstrate ulcerating lesions, but possibly from the lung. As I have said before, it is impossible to be certain about the point of origin of these malignant tumors.

A PHYSICIAN: There is no mention whether the mass did or did not move with respiration. If we could assume that it did move with the liver it would make a great deal of difference.

DR DONALD S KING: Dr Townsend remembers a case in which the tumor was primary above the diaphragm, with metastases below. The one that I had a few years ago was the other way around — primary in the stomach, with metastases to the nodes about the lung roots.

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DR WILLIAM CLARK: In an autopsy done several months ago there was primary cancer of the lung with metastases to a cirrhotic liver.

#### CLINICAL DIAGNOSIS

Carcinoma of stomach, with metastases to liver and lungs

#### DR TOWNSEND'S DIAGNOSIS

Malignant tumor, primary in liver, arising from pre-existing cirrhosis, with generalized metastases

#### ANATOMICAL DIAGNOSES

Hepatoma, with metastases to lungs, pancreas, kidneys and mediastinal and retroperitoneal lymph nodes

Cirrhosis of liver

Esophageal varices

Hydrothorax, bilateral

#### PATHOLOGICAL DISCUSSION

DR MALLORY: The autopsy on this patient showed a greatly enlarged liver with large and small tumor nodules jutting out all over the surface. Between the various tumor nodules, however, a few small areas of liver tissue could still be recognized, and

these areas were definitely cirrhotic. Besides the tumor in the liver, the pancreas was found completely replaced by tumor and there were metastases in the lungs. The presence of invasive neoplasm in the pancreas raised doubt at the time of autopsy concerning the nature of the tumor, but there was one point that I think is strong evidence in favor of a hepatoma: when one examined the liver from the posterior surface and looked at the hepatic vein, a tumor thrombus was seen to project from the mouth of the vein into the vena cava, and on examination of the rest of the liver all the hepatic veins were found to be filled with tumor thrombi. There are only two tumors that more or less regularly grow into veins in the form of gross thrombi. Hypernephroma is one of them, as you know, this frequently fills the renal vein and later the vena cava. Hepatoma is the other, indeed, it is not infrequent for a hepatoma to show growth up the hepatic vein into the vena cava and sometimes directly into the right auricle of the heart, which may become completely filled with tumor. On this basis I thought at the time of autopsy that the liver was the probable primary source of the tumor. Microscopically the sections do not help us a great deal further. They are consistent with a hepatoma but not particularly characteristic of it. The tumor was certainly undifferentiated, so that a positive histologic diagnosis is scarcely possible. To my eye it does look considerably more like a liver-cell tumor than a pancreatic tumor, and I think that the gross anatomic appearance and the massive venous invasion are enough to substantiate the diagnosis of hepatoma based on a pre-existing cirrhosis.

The terminal episode was almost certainly, as suggested, a rupture of an esophageal varix, since the stomach was filled with clotted blood. We were unsuccessful in demonstrating the point of rupture.

DR TOWNSEND: I should like to ask whether these varices can rapidly develop secondary to malignant disease or whether they take time, years, to develop?

DR MALLORY: On occasion we have seen esophageal varices for which we could determine no cause.

DR TOWNSEND: But is it not true that you usually do not see them associated with a liver full of metastatic cancer?

DR MALLORY: Almost never.

#### CASE 32202

#### PRESENTATION OF CASE

*First admission.* A thirty-year-old housewife entered the hospital because of leukorrhea and metrorrhagia of three months' duration.

The patient had had one child, a normal infant born eighteen months before admission after a long, difficult labor. On physical examination there was tenderness in both lower quadrants just above the

groin The large, hard cervix was fixed on the left The posterior lip was eroded, and there was a cauliflower shaped mass in the external os Biopsy revealed a Grade III epidermoid carcinoma of the cervix A chest film, an abdominal film and an intravenous pyelogram were normal A program of x-ray and radium treatment was outlined in preparation for surgical excision of the tumor, and the patient was discharged on the third hospital day

*Second admission* (six weeks later) In the interval the patient had received a total of 3000 r by the million-volt machine directed to the anterior and posterior cervix The vaginal discharge had ceased

On readmission the physical findings were unchanged, except for induration and fixation of the upper posterior vaginal wall, which had not been observed previously One hundred milligrams of radium were sutured in the cervical canal on the second and seventh hospital days, and five 10-mg needles were placed around the periphery and left for a total dose of 2250 millicurie hours after each operation She was discharged on the eighth day

*Final admission* (eighteen months later) Following her last entry the patient gained weight and vigor and felt well for the first six months She then began to have short episodes of diarrhea, characterized by the passage of five or six liquid mucous and blood-streaked stools daily, which were fairly well controlled by paregoric Two months before admission she became weak and anorexic and had to go to bed Two weeks later she became nauseated and vomited about every other meal By the end of three weeks she had become extremely anorexic and weak The urine was dark, and the stools were light The abdomen felt so bloated that it interfered with respiration on lying down One month prior to admission the patient entered another hospital, where the hemoglobin was found to be 22 per cent and she was treated with eight transfusions After the fourth transfusion, she felt chilly and it was noted that her skin was yellow The remaining transfusions proceeded uneventfully The patient stayed in the hospital ten days and then returned home For about ten or twelve days after its onset the jaundice became deeper and the urine became darker, iron therapy obscured the color of the stool After that the jaundice decreased and the urine was lighter but did not become normal Hemorrhoids had developed within the three-month period before admission The night before admission the patient drank a glassful of water and five minutes later vomited it Five minutes after that she vomited again, the vomitus being light red

On physical examination the patient was emaciated and mildly icteric The heart seemed normal except for a Grade II apical systolic murmur There were flatness, absent tactile fremitus and whispered voice sounds and diminished spoken voice sounds at the right base The abdomen was protuberant

and firm and seemed to be full of fluid The skin of the abdomen was mottled The vagina was contracted and firm The cervix and vaults were obliterated Moderate sacral and ankle edema was present There were external hemorrhoids

The temperature was 98.6°F, the pulse 104, and the respirations 20 The blood pressure was 112 systolic, 70 diastolic

The red-cell count was 2,200,000, with 5.5 gm of hemoglobin The white cell count was 4800, with 90 per cent neutrophils The urine specific gravity was 1.010, and there was a +++ test for bile Urobilinogen was demonstrated in a dilution of 1:32 The urinary sediment was normal The stools repeatedly gave +++ guaiac tests Other laboratory findings were as follows: total protein, 5.4 gm, with 3.2 gm of albumin and 2.2 gm of globulin, nonprotein nitrogen, 15 mg, van den Bergh reaction, 7.7 mg direct and 10.3 mg indirect cephalin-flocculation test, negative at twenty-four hours and + at forty-eight hours, prothrombin time, 43 seconds (normal, 19 to 22 seconds), phosphorus, 2.5 mg, alkaline phosphatase, 29.7 units; and cholesterol esters, 79 mg On x-ray examination the liver appeared enlarged and the flanks were bulging There was a small ring shadow in the right upper quadrant Both costophrenic angles were obliterated, evidently by small amounts of fluid The right leaf of the diaphragm was irregular and elevated, and there was a translucent area between it and the liver In the lateral projection there was a translucent area between the diaphragm and the liver, as well as a wedge-shaped area of density along the midanterior chest wall, whether the latter was on the right or left could not be determined A barium enema revealed two areas of constriction of the ileum, each 2 cm in length One was approximately 16 cm proximal to the ileocecal valve, and the other 8 cm proximal to the first The colon was normal

On the second hospital day the temperature rose to 101°F and thereafter spiked from 100 to 102°F daily The next day the red-cell count was 1,340,000 Within a week pain developed in the right shoulder and the feet became extremely tender and swollen The esophagus, stomach and duodenum appeared normal in a gastrointestinal series performed at that time A peritoneoscope was introduced, and 2500 cc of yellow ascitic fluid was withdrawn The liver appeared to be large and smooth and contained innumerable blue spots, which were thought to be consistent with passive congestion, the spleen was also enlarged No metastases were seen in the abdomen or pelvis The fluid had a specific gravity of 1.007 and was negative for tumor cells On the fifteenth day pain developed in the right shoulder and axilla, and several hours later 750 cc of red blood was vomited The pain disappeared Three days later 10 cc of blood was vomited There were no other episodes of hematemesis, but many clots

were passed by rectum. Numerous transfusions of whole blood brought the hemoglobin up to 10 gm, but the prothrombin time was not much shortened. The van den Bergh reaction gradually rose to 14.5 mg direct and 18.3 mg indirect, and there was accentuation of the edema of the lower extremities, the superficial abdominal veins became prominent. In the fifth hospital week there was a decided change for the worse. The jaundice deepened, and the abdomen distended with fluid. Edema of the lower extremities and dependent parts became severe. The total protein was 5.4 gm per 100 cc. Pain was constant in the region of the right anterior axillary fold. The superficial veins became more prominent. The liver, which had been felt after the paracentesis for the first time, extended three fingerbreadths below the costal margin and was tender. The spleen was palpable. The breath smelled mousey.

Two weeks later she began to be confused. Six liters of yellow-brown fluid was withdrawn from the abdomen. The van den Bergh reaction was 20 mg direct and 25.9 indirect, and the phosphorus and alkaline phosphatase were 4.1 mg and 73.1 units per 100 cc, respectively. At the end of two months she was stuporous most of the time. She died on the sixty-third hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR WILMAN RICHARDSON: The total length of life from this woman's first admission was approximately twenty-one and a half months.

I am not going to discuss the treatment of carcinoma of the cervix. I simply wish to point out that she received a considerable amount of radiation, sufficient, I think, in a number of cases to produce real cure. Is that correct, Dr Lingley?

DR. JAMES R. LINGLEY: Yes.

DR. RICHARDSON: "The urine was dark, and the stools were light." I might bring up the question, Was this due to jaundice? It is of some importance. I think that it probably was the onset of jaundice although one cannot be sure.

The hemoglobin was 22 per cent, which is extremely low. If it were a normochromic anemia, the red-cell count would be around one million.

"After the fourth transfusion the skin was yellow." I shall again bring out the point that we had a suggestion that jaundice was present before she was given any transfusions. The timing of the transfusions is not given but I think we can assume that they were given in a relatively short space of time. I do not know whether that is a fair assumption.

A loud systolic murmur in a thirty-year-old woman is not normal, although it is difficult to rule out physiologic systolic murmurs on the basis of the loudness of the murmur.

I wish to emphasize that this woman had a low white-cell count (5000), with 90 per cent neutrophils. That is an unusual finding and is consistent

with severe sepsis. If one had a record of the character of the cells one might be able to say definitely that this was severe sepsis. The reason that it is not in the protocol is that very likely no one looked to see if the cells showed signs of toxic sepsis.

"Urobilinogen was demonstrated in a dilution of 1:32." In a case I discussed recently I brought out the point that this is definite evidence that bile was at least reaching the gastrointestinal tract.

Another thing that I keep talking about is that we are told about guaiac tests on the stools but there is no record about their color. It is even difficult to get to look at one on the ward. It would be of some interest to know whether the stools were brown or clay colored. I take it that they were brown.

There was slight reduction in the albumin-globulin ratio. The quite low reading of the non-protein nitrogen may have been due to the fact that this patient had liver disease. The phosphorus was slightly elevated, and the phosphatase was high.

Perhaps the small ring shadow in the right upper quadrant on x-ray examination suggests gallstones. Let us look at the films now. The area above the diaphragm and these intestinal shadows interest me more than anything else.

DR LINGLEY: On this abdominal film I think that the liver is enlarged. I cannot see the ring shadow that was mentioned in the record. The area of the gall bladder looks perfectly clear. This is the film of the chest showing the area of rarefaction described as being beneath the diaphragm. If it is beneath the diaphragm, it means free air in the peritoneal cavity. I am inclined to doubt this, because I cannot see it in the lateral view. I wonder if the upper line interpreted as diaphragm is not just a plaque-like focus of atelectasis in the lung with normal aerated lung beneath it. These are the films of the colon showing the two areas of constriction in the ileum. They are perfectly smooth and have the appearance of benign strictures.

DR CHESTER M. JONES: Could this picture be due to radiation?

DR LINGLEY: Very possibly.

DR RICHARDSON: I think that it is.

Pain in the right shoulder could have been due to diaphragmatic irritation.

We do not know whether this patient received some form of vitamin K, presumably she did. If so, it apparently did not cause a decrease in the prothrombin time. The bleeding that occurred may be explained on the basis of prothrombin lack, it is not necessary to postulate a demonstrable ulcerative lesion. The fact that the prothrombin time was not shortened by blood transfusions would not be remarkable if blood-bank blood, not fresh blood, was used. Blood is not much good to provide prothrombin after forty-eight hours. Would you agree to that, Dr Jones?

DR JONES: I feel the same way. The fresher the blood the better.

DR RICHARDSON Shall we try to explain the entire picture on the basis of one illness and the results of that illness, or do we have to search around for many incidental diseases? In the older age group the latter is often profitable. This was a relatively young person, and it is better to explain it all on one disease if we can. We might go afield, especially if there were gallstones, and think of neoplasm of the biliary system with involvement of the liver, but I shall not bring that in. The other thing that I have already hinted at is the question whether this patient had a transfusion hepatitis. I assume that the jaundice came on before the transfusion or at least appeared too soon afterward to be the result of transfusion, so I shall also rule that out.

We still have to consider the question whether this patient had acute hepatitis or subacute hepatitis going on to liver degeneration. It seems to me that there never was the acute severe febrile onset that so many of these patients with severe hepatitis have. The whole progress of the disease seems to have been chronic, and I shall rule out an acute hepatitis as being by itself the cause of the liver disease. I cannot rule out the possibility of secondary hepatic degeneration.

So then I come back to the fact that this was all the result of a single process, and of course the easiest thing to do is to say that this patient had metastatic disease from carcinoma of the cervix and try to link up the whole thing on that basis. It seems to me that a tumor of the cervix is much likelier, especially at the beginning, to extend locally rather than to produce such a widespread picture, which flared up more or less suddenly. If she had recurrence of the disease in the pelvis, I should have expected that she would have had local symptoms, especially those due to involvement of the ureters, hydronephrosis and that sort of thing. I am therefore inclined to doubt that it was due to carcinoma of the cervix, and that brings up the question Dr Jones mentioned.

Did she have a severe x-ray enteritis or x-ray effect on the bowel? It would seem to me that, considering the amount of treatment that she had close to that area, one might say that this lesion was due to the effect of radiation therapy. This might account for the diarrhea and the gastrointestinal symptoms, but it would not account for everything. The process might have gone on further to produce fibrosis, with ulceration and actual perforation of the bowel. If we suppose that it occurred gradually, so as not to produce generalized peritonitis, it would account for sepsis in the abdomen, which was not discovered. It seems to me quite likely that this patient actually had sepsis in the abdomen, with infection of the portal and mesenteric venous system and multiple small abscesses in the liver.

What more? The patient had a Grade II systolic murmur, which brought to my mind a terminal bac-

terial endocarditis. Many patients with chronic illness, if they have a cardiac lesion, end up with a terminal bacterial endocarditis, and that might account for the wedge-shaped shadow in the lung. I think that this patient might have had an infarction in the lung and that of course might well have come from a peripheral vein, and it might also have come from the heart. I do not want to prolong this discussion. I will say, therefore, that I believe that this patient did not have metastatic disease from the original tumor. I think that she had an x-ray enteritis, as a result of which she had what might be called a septic phlebitis, with multiple liver abscesses followed by secondary liver degeneration, and that she died of liver failure.

DR TRACY B MALLORY Are there any suggestions or alternative diagnoses?

DR WALTER BAUER Why could it not all be explained on the basis of an infectious hepatitis that began before the transfusions were given? The clinical course is not against such an interpretation. I admit that 90 per cent neutrophils in the presence of a white-cell count of 5000 is most unusual, although there have been some verified cases of infectious hepatitis with such a leukocyte count. Although Dr Richardson's diagnosis may be correct, we must bear in mind other possibilities.

DR JONES I agree with Dr Richardson that this woman was jaundiced before transfusion. She already had a profound anemia, and after eight transfusions she still had a profound anemia. I do not believe that an anemia of that degree was solely on the basis of an ulcerative lesion in the bowel. It could have been, but I doubt it. Another thing that I should like to comment on is the peritoneal fluid that was withdrawn some days before death — some days before she had more abdominal pain, it was a straight transudate, with a specific gravity of 1.007, which is against an inflammatory process in the abdominal cavity. Finally, I think that the signs of pressure or biliary obstruction are striking, even if there is no comment about the color of the stools. The phosphatase is striking. One can get a phosphatase that high in intrahepatic disease with jaundice, but it is not at all frequent, in fact it is quite unusual. I believe that this points to an obstructive lesion that was extrahepatic.

DR RICHARDSON I meant to mention the phosphatase. I have laid stress on it in other cases but thought that I would throw it overboard this time.

DR J H MEANS I can recall one patient who was here about a year ago who had a good many points in common with this woman except that the patient was a man who did not have a cancer to start with. The rest of the picture was similar, including the blood picture, and at autopsy he turned out to have just what Dr Richardson has described.

DR JONES This degree of jaundice is rather intense for pylephlebitis, and there is no story of chills and fever

#### CLINICAL DIAGNOSIS

Carcinoma of cervix, with generalized metastases

#### DR RICHARDSON'S DIAGNOSES

Radiation enteritis

Pylephlebitis

Multiple liver abscesses

Terminal bacterial endocarditis?

#### ANATOMICAL DIAGNOSES

Metastases of carcinoma of cervix to liver, lung and mesentery, with obstruction of vena cava, portal vein, right branch of hepatic artery and hepatic duct.

Esophageal varices, with rupture

Anasarca

Splenomegaly

Obstructions (two) of ileum, due to tumor nodules in mesentery

Jaundice, severe

#### PATHOLOGICAL DISCUSSION

DR MALLORY The autopsy showed that this was entirely due to one disease — cancer of the cer-

vix The surface of the liver, as described at peritoneoscopy, was perfectly smooth, but on section the liver was about 60 or 70 per cent replaced by tumor This tumor had grown directly into the vena cava, and the tumor and secondary thrombosis had produced a complete obstruction of the cava It had also grown down the lymphatic vessels around the portal vein, the common bile duct and the hepatic artery, so that the portal vein, the bile duct and one branch of the hepatic artery were occluded by external pressure of the tumor There were some metastases to the lung, which were probably due to tumor emboli from this mass in the cava The heart, despite the murmurs, was completely negative The ileum was occluded in two spots by linking around tumor masses in the mesentery It showed no evidence of radiation enteritis

On many occasions in these exercises we have pointed out that metastatic tumor to the liver does not produce portal hypertension In this case the enlarged spleen, weighing 500 gm, and the presence of well marked esophageal varices leave little doubt that it existed The obstruction, however, was apparently not produced within the liver but by the extension of the tumor into the tissues about the hilus, with constriction of the extrahepatic portal vein

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## NATIONAL HOSPITAL DAY

ON MAY 12 the hospitals of this country observed National Hospital Day. Having satisfactorily met increasing demands on their facilities during the years of the war in spite of curtailments in personnel, equipment and supplies, they are now faced with the tremendous task of furnishing adequate facilities and care to an even greater number of people. As Dr. Peter D. Ward, president of the American Hospital Association has stated:

This does not mean that more people will be ill, but simply that the public has become more hospital-minded. Also, the benefits of Blue Cross have made hospital care available to more people. As preventive medicine has come of age, the hospital no longer signifies a place for final and drastic measures, rather it is a place for health protection, where minor as well as major ailments may find alleviation.

It might be added that still another factor is involved, namely, that miracles in the handling of

certain types of medical and surgical cases have permitted the successful hospital treatment of patients who were formerly told that nothing could be done for them.

Certain of the voluntary hospitals, whose total assets comprise two thirds of the value of all general hospitals in this country, have already made plans for new construction, but many other things must be accomplished to meet this challenge. These include hospital surveys, licensing systems, increased availability of prepaid hospital and medical-care insurance and the establishment of health centers. If a voluntary system of medical care is to continue, these hospitals must have the confidence and the enthusiastic support of the public and the medical profession. Indeed, financial assistance from state governments, supplemented, if necessary, by federal grants-in-aid, will probably be required for the successful accomplishment of this program, which has much to do with the health of the Nation.

## SIXTY YEARS OF NURSING SERVICE

It is fitting that the celebration of the sixtieth anniversary of the establishment of the Visiting Nurse Association of Boston, which was held during Public-Health Nurse Week in April, should receive recognition by the medical profession.

Beginning in 1886, under the name Instructive District Nursing Association, with two nurses, it was employing one hundred and fifty nurses on its fiftieth anniversary, and it has always found opportunities far greater than its financial support has justified an attempt to meet. Throughout these years it has been a most valuable and valued ally of the medical profession and has demonstrated in its own field the indispensable nature of the contribution of the public-health nurse, not only in caring for the sick but in advancing civilization through the prevention of disease.

True to its central purpose, as the original name made explicit, it has been an educational institution, and although the first approach is through the bedside nursing of patients who, except in emergency, are under the supervision of a physician, its unit of major interest is the family. It renders family health service. Here an important approach is by



of problems of individual and family nutrition, and this raises the question of making, using and saving to a budget. Although this aspect of the work is time-consuming, fundamental lessons in household economics are taught.

The Association renders a community service to people of all classes. About 15 per cent of the patients pay the full cost, and 7 per cent pay part of the cost. The full cost in 30 per cent of the cases is paid for by certain insurance companies. In slightly less than 50 per cent of the cases no money is collected. Since the establishment of the Boston Community Fund, the Association has been a participating agency.

It started the first school in the United States for the training of visiting nurses, which was later taken over by Simmons College, and it continues to offer an opportunity for field work to students. Its work is carried on all over the City of Boston, and last year a total of 155,200 calls were made on 22,885 persons. It employs supervisors specially trained in nutrition, mental hygiene, social hygiene, occupational therapy, physical therapy and maternity care and in the administration of its twelve districts. Although the number of cases given care at confinement is relatively small, since so many patients go to hospitals, prenatal care was administered to 5000 women during the past year.

The scope of the Association's work cannot be described briefly, and it is impossible to measure the benefits of the ministrations of its devoted nurses through these sixty years. We congratulate the community on having in its midst such a strong and vigorous organization, and we extend, on behalf of the medical profession, best wishes for even greater usefulness in the future.

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

**GUNTER** — Fred C. Gunter, M.D., of Belmont, died April 24. He was in his fifty-fifth year.

Dr. Gunter received his degree from Tufts College Medical School in 1914. He was a veteran of both world wars. He was a specialist in internal medicine, being particularly interested in cardiac diseases, and was formerly chief of staff of the Robert Breck Brigham Hospital, of Boston. Dr. Gunter was on the courtesy staff of the Brooks Hospital, Brookline, and was a fellow of the American Medical Association.

His widow, a son and his mother survive.

**METZGER** — Butler Metzger, M.D., of Lynn, died April 25. He was in his seventy-third year.

Dr. Metzger received his degree from Harvard Medical School in 1897. He was on the staff of the Union Hospital, Lynn. He was a fellow of the American Medical Association.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MARCH 1946

#### RÉSUMÉ

DISEASES	MARCH 1946	MARCH 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	2	4	1
Chancroid	1	4	*
Chicken pox	1391	1320	1471
Diphtheria	20	20	14
Dog bite	1024	783	733
Dysentery bacillary	14	4	4
German measles	680	224	225
Gonorrhea	424	459	327
Granuloma inguinale	1	1	*
Lymphogranuloma venereum	2	2	*
Malaria	62	76	1
Measles	3085	624	3245
Meningitis meningococcal	12	22	21
Meningitis Pfeiffer bacillus	4	3	3
Meningitis pneumococcal	5	1	6†
Meningitis staphylococcal	0	0	0†
Meningitis streptococcal	0	0	0†
Meningitis other forms	1	0	3†
Meningitis undetermined	2	5	10†
Mumps	831	2789	1349
Pneumonia lobar	243	257	423
Salmonella infections	8	8	3
Scarlet fever	894	1692	1457
Syphilis	482	412	462
Tuberculosis, pulmonary	282	230	262
Tuberculosis other forms	23	20	20
Typhoid fever	3	1	2
Undulant fever	5	5	3
Whooping cough	594	853	874

\*Made reportable December, 1943

†Four year average

#### COMMENT

Diphtheria, German measles and pulmonary tuberculosis were reported at figures above their seven-year median. The slight increase in the last is undoubtedly attributable to state-wide case-finding programs. Salmonella and bacillary dysentery cases were also reported at higher figures. Dog bite reached a record high figure for the month. The high incidence of malaria is due to its appearance in veterans from malaria-infested zones.

Reported at a record low figure was lobar pneumonia. Measles was reported at a figure below the seven-year median, in spite of a marked national increase. Also at figures below the seven-year medians were chicken pox, mumps, scarlet fever, whooping cough and meningococcal meningitis.

#### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from Holyoke, 1, Lawrence, 1, Malden, 1, total, 3.

Anterior poliomyelitis was reported from Everett, 1, Spencer, 1, total, 2.

Diphtheria was reported from Boston, 10, Cambridge, 1, Dracut, 1, Falmouth, 1, Ipswich, 1, Lowell, 1, Medford, 1, Melrose, 2, Taunton, 2, total, 20.

Dysentery, bacillary, was reported from Boston, 1, Marblehead, 1, Wrentham (State School), 12, total, 14.

Encephalitis, infectious, was reported from Worcester, 1, total, 1.

Malaria was reported from Boston, 11, Brockton, 2, Brookfield, 1, Brookline, 1, Cambridge, 4, Chelsea, 1, Dartmouth, 1, Gardner, 1, Holbrook, 1, Holliston, 1, Lawrence, 1, Lynn, 1, Malden, 3, Medford, 2, New Bedford, 1, Newton, 2, Peabody, 3, Pittsfield, 2, Quincy, 1, Rockport, 1, Somerville, 2, Springfield, 2, Stoneham, 1, Stoughton, 2, Tyngsboro, 1, Waltham, 1, Waltham Regional Hospital, 1, Warren, 2, Westfield, 1, Worcester, 7, total, 62.

Meningitis, meningococcal, was reported from Boston, 4, Brockton, 1, Clarksburg, 1, Everett, 1, Fall River, 1, Lawrence, 1, Lowell, 1, Medford, 1, Somerville, 1, total, 12.

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## NATIONAL HOSPITAL DAY

ON MAY 12 the hospitals of this country observed National Hospital Day. Having satisfactorily met increasing demands on their facilities during the years of the war in spite of curtailments in personnel, equipment and supplies, they are now faced with the tremendous task of furnishing adequate facilities and care to an even greater number of people. As Dr. Peter D. Ward, president of the American Hospital Association has stated:

This does not mean that more people will be ill, but simply that the public has become more hospital-minded. Also, the benefits of Blue Cross have made hospital care available to more people. As preventive medicine has come of age, the hospital no longer signifies a place for final and drastic measures, rather it is a place for health protection, where minor as well as major ailments may find alleviation.

It might be added that still another factor is involved, namely, that miracles in the handling of

certain types of medical and surgical cases have permitted the successful hospital treatment of patients who were formerly told that nothing could be done for them.

Certain of the voluntary hospitals, whose total assets comprise two thirds of the value of all general hospitals in this country, have already made plans for new construction, but many other things must be accomplished to meet this challenge. These include hospital surveys, licensing systems, increased availability of prepaid hospital and medical-care insurance and the establishment of health centers. If a voluntary system of medical care is to continue, these hospitals must have the confidence and the enthusiastic support of the public and the medical profession. Indeed, financial assistance from state governments, supplemented, if necessary, by federal grants-in-aid, will probably be required for the successful accomplishment of this program, which has much to do with the health of the Nation.

## SIXTY YEARS OF NURSING SERVICE

It is fitting that the celebration of the sixtieth anniversary of the establishment of the Visiting Nurse Association of Boston, which was held during Public-Health Nurse Week in April, should receive recognition by the medical profession.

Beginning in 1886, under the name Instructive District Nursing Association, with two nurses, it was employing one hundred and fifty nurses on its fiftieth anniversary, and it has always found opportunities far greater than its financial support has justified an attempt to meet. Throughout these years it has been a most valuable and valued ally of the medical profession and has demonstrated in its own field the indispensable nature of the contribution of the public-health nurse, not only in caring for the sick but in advancing civilization through the prevention of disease.

True to its central purpose, as the original name made explicit, it has been an educational institution, and although the first approach is through the bedside nursing of patients who, except in emergency, are under the supervision of a physician, its unit of major interest is the family. It renders family health service. Here an important approach is by

of problems of individual and family nutrition, this raises the question of making, using and applying to a budget. Although this aspect of the work is time-consuming, fundamental lessons in household economics are taught.

The Association renders a community service to people of all classes. About 15 per cent of the patients pay the full cost, and 7 per cent pay part of the cost. The full cost in 30 per cent of the cases is paid for by certain insurance companies. In slightly less than 50 per cent of the cases no money is collected. Since the establishment of the Boston Community Fund, the Association has been a participating agency.

It started the first school in the United States for the training of visiting nurses, which was later taken over by Simmons College, and it continues to offer an opportunity for field work to students. Its work is carried on all over the City of Boston, and last year a total of 155,200 calls were made on 22,885 persons. It employs supervisors specially trained in nutrition, mental hygiene, social hygiene, occupational therapy, physical therapy and maternity care and in the administration of its twelve districts. Although the number of cases given care at confinement is relatively small, since so many patients go to hospitals, prenatal care was administered to 5000 women during the past year.

The scope of the Association's work cannot be described briefly, and it is impossible to measure the benefits of the ministrations of its devoted nurses through these sixty years. We congratulate the community on having in its midst such a strong and vigorous organization, and we extend, on behalf of the medical profession, best wishes for even greater usefulness in the future.

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

**GUNTER** — Fred C Gunter, M.D., of Belmont, died April 24. He was in his fifty-fifth year.

Dr Gunter received his degree from Tufts College Medical School in 1914. He was a veteran of both world wars. He was a specialist in internal medicine, being particularly interested in cardiac diseases, and was formerly chief of staff of the Robert Breck Brigham Hospital, of Boston. Dr Gunter was on the courtesy staff of the Brooks Hospital, Brookline, and was a fellow of the American Medical Association.

His widow, a son and his mother survive.

**METZGER** — Butler Metzger, M.D., of Lynn, died April 25. He was in his seventy-third year.

Dr Metzger received his degree from Harvard Medical School in 1897. He was on the staff of the Union Hospital, Lynn. He was a fellow of the American Medical Association.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MARCH, 1946

#### RÉSUMÉ

DISEASES	MARCH 1946	MARCH 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	2	4	1
Chancroid	1	4	*
Chicken pox	1391	1320	1471
Diphtheria	20	20	14
Dog bite	1024	783	733
Dysentery, bacillary	14	4	4
German measles	680	224	225
Gonorrhea	424	459	327
Granuloma inguinale	1	1	*
Lymphogranuloma venereum	2	2	*
Malaria	62	76	1
Measles	3085	624	3245
Meningitis, meningococcal	12	22	21
Meningitis, Pfeiffer bacillus	4	3	1
Meningitis, pneumococcal	5	1	6†
Meningitis, staphylococcal	0	0	0†
Meningitis, streptococcal	1	0	0†
Meningitis, other forms	1	0	3†
Meningitis, undetermined	2	5	10†
Mumps	831	2789	1349
Pneumonia, lobar	243	257	423
Salmonella infections	8	8	3
Scarlet fever	894	1692	1457
Syphilis	482	412	462
Tuberculosis, pulmonary	232	230	262
Tuberculosis, other forms	3	1	2
Typhoid fever	5	5	3
Undulant fever	594	853	874
Whooping cough			

\*Made reportable December 1943

†Four year average

#### COMMENT

Diphtheria, German measles and pulmonary tuberculosis were reported at figures above their seven-year median. The slight increase in the last is undoubtedly attributable to state-wide case-finding programs. Salmonella and bacillary dysentery cases were also reported at higher figures. Dog bite reached a record high figure for the month. The high incidence of malaria is due to its appearance in veterans from malaria-infested zones.

Reported at a record low figure was lobar pneumonia. Measles was reported at a figure below the seven-year median, in spite of a marked national increase. Also at figures below the seven-year medians were chicken pox, mumps, scarlet fever, whooping cough and meningococcal meningitis.

#### GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Actinomycosis was reported from Holyoke, 1, Lawrence, 1, Malden, 1, total, 3.

Anterior poliomyelitis was reported from Everett, 1, Spencer, 1, total, 2.

Diphtheria was reported from Boston, 10, Cambridge, 1, Dracut, 1, Falmouth, 1, Ipswich, 1, Lowell, 1, Medford, 1, Melrose, 2, Taunton, 2, total, 20.

Dysentery, bacillary, was reported from Boston, 1, Marblehead, 1, Wrentham (State School), 12, total, 14.

Encephalitis, infectious, was reported from Worcester, 1, total, 1.

Malaria was reported from Boston, 11, Brockton, 2, Brookfield, 1, Brookline, 1, Cambridge, 4, Chelsea, 1, Dartmouth, 1, Gardner, 1, Holbrook, 1, Holliston, 1, Lawrence, 1, Lynn, 1, Malden, 3, Medford, 2, New Bedford, 2, Newton, 2, Peabody, 3, Pittsfield, 2, Quincy, 1, Rockport, 1, Somerville, 2, Springfield, 2, Stoneham, 1, Stoughton, 2, Tyngsboro, 1, Waltham, 1, Waltham Regional Hospital, 1, Warren, 2, Westfield, 1, Worcester, 7, total, 62.

Meningitis, meningococcal, was reported from Boston, 4, Brockton, 1, Clarksburg, 1, Everett, 1, Fall River, 1, Lawrence, 1, Lowell, 1, Medford, 1, Somerville, 1, total, 12.

Meningitis, Pfeiffer-bacillus, was reported from Everett, 1, Petersham, 1, Springfield, 1, Wareham, 1, total, 4

Meningitis, pneumococcal, was reported from Fall River, 1, Lynn, 1, Marblehead, 1, Winthrop, 1, Worcester, 1, total, 5

Meningitis, other forms, was reported from Philipston, 1, total, 1

Meningitis, undetermined, was reported from Camp Edwards, 1, Nantucket, 1, total, 2

Salmonella infections were reported from Boston, 2, Granby, 1, Lynn, 1, Newton, 1, Revere, 1, Southampton, 2, total, 8

Septic sore throat was reported from Attleboro, 1, Boston, 7, Medford, 1, Merrimac, 2, Newton, 1, Orange, 1, Williamstown, 1, total, 14

Trachoma was reported from Milton, 1, total, 1

Trichinosis was reported from Adams, 3, Boston, 1, total, 4

Typhoid fever was reported from Fall River, 1, Lawrence, 1, Norwood, 1, total, 3

Undulant fever was reported from Adams, 1, East Longmeadow, 1, Melrose, 1, Nantucket, 1, Southbridge, 1, total, 5

of Walter Dodd and of the late "Joe" Godsoe, — his assistant at that time, — who died on February 8

I well remember an incident that may have been prophetic. On the morning after Walter Dodd made his first experiments with the Crookes's tube he gave a brief demonstration with the fluoroscope before several physicians and surgeons who were attached to the hospital at that time. Among them was the late Dr. Maurice Richardson who, after looking at his hand, pulled out an old wallet from his hip pocket, held it in his hand before the fluoroscope and remarked, "I think that I can see more in this than I had realized," still holding the purse. We laughed, of course, thinking that he was referring to the amount of cash in coins in the purse, but I have since wondered if he were not looking much farther ahead than we realized at the time.

FRANK T. WOODBURY, M.D.

21 Chestnut Street  
Wakefield, Massachusetts

## NOTICES

### ANNOUNCEMENTS

Dr. Herman Beigelman announces his return from military service and the reopening of his office for the practice of medicine at 139 Washington Street, Weymouth

Dr. Joseph Factor, having returned from military service, is resuming the practice of obstetrics and gynecology at 45 Bay State Road, Boston

Dr. Joseph A. Famighetti announces his return from military service and the opening of his office for the general practice of medicine at 56 Saratoga Street, East Boston

Dr. Roy E. Mabrey announces his return to the practice of surgery at 270 Commonwealth Avenue, Boston

Dr. Louis Zetzel, having returned from military service, announces the reopening of his office at 53 Bay State Road, Boston, for the practice of internal medicine and gastroenterology

### HARVARD MEDICAL ALUMNI ASSOCIATION

The annual meeting and dinner of the Harvard Medical Alumni Association will be held at the Sir Francis Drake Hotel, San Francisco, on July 3, during the period when the annual meeting of the American Medical Association is in session

### MASSACHUSETTS MEDICO-LEGAL SOCIETY

The annual meeting of the Massachusetts Medico-Legal Society will be held at the Hotel Statler, Boston, on Wednesday, May 22, at 2:00 p.m.

#### PROGRAM

Report of Secretary  
Report of Treasurer  
Unfinished Business

#### New Business

Report of Nominating Committee, Dr. Brickley, chairman  
Election of Officers  
Nomination of Standing Committee  
Election of New Members

#### Scientific Program

Delayed Death after Gunshot Wound of Heart  
Dr. C. H. Keene  
Atypical Case of Suicide Dr. Richard Fort  
Fatal Spinal-Cord Injury without Fracture or Demonstrable Dislocation of Spine Dr. I. W. Richardson  
An Unusual Case of "Walking Pneumonia" Dr. P. H. Leavitt

(Notices continued on page xv)

## MISCELLANY

### NOTES

The Boston Surgical Society awarded the Henry Jacob Bigelow Medal to Dr. Frank H. Lahey on May 10. Dr. Lahey gave an address entitled "Surgery of the Thyroid," following which he was presented with the Bigelow Medal by the president of the society, Dr. Donald Munro.

The Board of Managers of the Quincy City Hospital have recently announced that Dr. Ensio K. F. Ronka was appointed director of the hospital on April 1.

## CORRESPONDENCE

### MORE ABOUT BACTERIOLOGIC LABORATORIES

To the Editor: I was much interested in the letter from Dr. Wails, Commissioner of Health of Worcester, Massachusetts, regarding health department bacteriological laboratories, which appeared in the March 14 issue of the *Journal*.

It might be interesting to your readers to know that the City of Boston started the examination of throat cultures for diphtheria in November, 1894. During that and the following month, 1002 cultures were examined, with 246 positives. This work was performed at the Harvard Medical School by Dr. McCollum, physician to the Board of Health. The 1894 report reads, "All physicians were invited to take cultures from throats where diphtheria was suspected, and for their convenience, culture tubes in cases were provided and stations were established at drugstores, where physicians could obtain tubes for cultures." Ten stations were established, one of which is still in existence.

November, 1894, also saw the beginning of the manufacture of diphtheria antitoxin by the Boston Health Department. This work was performed on Gallup's Island, in Boston Harbor, by Dr. Harold Ernst, of Harvard Medical School, assisted by Dr. C. G. Page and Dr. S. A. Hopkins. It was not until 1898 that the Commonwealth took over this work.

When I first read Dr. Wails's letter, without annual reports at hand, it immediately came to mind that perhaps Boston had a little something on Worcester, but as can be gathered from this letter, the Oscar will have to be given to Worcester by two months.

FREDERICK J. BAILEY, M.D.  
Health Commissioner

Health Department  
Haymarket Square  
Boston 14

### FIRST USE OF X-RAYS IN BOSTON

To the Editor: March marked the conclusion of fifty years since Walter Dodd made his first experiments in the use of a Crookes's tube at the Massachusetts General Hospital. I believe that the occasion warrants at least a brief mention

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PAPRIS, *Assistant Editor*

### CASE 32211

#### PRESENTATION OF CASE

A forty-six-year-old carpenter entered the hospital because of abdominal pain and vomiting.

The patient had been in apparent good health until two years before his last admission, when he had a two-day bout of severe crampy periumbilical nonradiating pain accompanied by nausea and vomiting. The pain was sudden in onset and required hospitalization for ten days. It bore no relation to meals and was not relieved by soda or food. He was discharged from the hospital on a diet. Eight months later he had a similar episode, which lasted intermittently for about three weeks and was associated with marked constipation. At that time he also had pleurisy and was hospitalized for one month. After discharge he continued to have a cough and to raise sputum, and for these reasons he was admitted to this hospital. A left lower lobe lobectomy was performed at that time for lung abscesses. While in the hospital he had another attack of abdominal pain. Physical examination of the abdomen, as well as a gastrointestinal series and a barium enema, was negative. Following the chest operation another abscess developed in the lingula, which yielded satisfactorily to penicillin treatment. The patient then gained weight and was completely asymptomatic until the month before admission, when he again had two attacks of periumbilical cramps, followed by vomiting after three to four hours. The pain was severe enough to require sedation with morphine. A Graham test, gastrointestinal series and barium enema, done at a local hospital, were reported as negative. At no time were the attacks accompanied by jaundice, melena, diarrhea or hematemesis. The appetite remained fair.

Physical examination revealed a well developed and well nourished man apparently in no acute distress. The heart was normal. The breath sounds were diminished at the left base. The abdomen was tender to pressure in the lower quadrants, but no masses were felt. Peristalsis was normal and active.

The temperature, pulse and respirations were normal. The blood pressure was 128 systolic, 70 diastolic.

Examination of the blood showed a hemoglobin of 12 gm per 100 cc. The white-cell count was 7100. The nonprotein nitrogen was 31 mg per 100 cc. The chloride was 104 milliequiv per liter, and the total serum protein was 5.8 gm per 100 cc. The serum amylase was 30 units per 100 cc. The urine was normal. The stools were guaiac negative on repeated examinations.

X-ray examination of the chest showed the mediastinum retracted to the left. The left leaf of the diaphragm was elevated, and the left costophrenic angle was deformed, apparently by old adhesions. Scattered bits of opaque material remained on the left side, and there were several areas in the left lower chest in which the lung markings could not be traced. A flat film of the abdomen showed a large amount of gas and fecal material in the colon. There were also gas-filled loops of small intestine. A gastrointestinal series with hourly films revealed a rounded extrinsic pressure defect of the duodenal bulb, which was probably due to the gall bladder. The stomach emptied normally. There was a peculiar widening and crowding of the mucosal markings in the jejunum that was somewhat suggestive of an intussusception led by a small tumor mass. A later film, however, showed that the head of the barium column was approaching the splenic flexure, with the barium distributed throughout the right colon and ileum. The jejunum was empty on the four-hour film. The ileum appeared wider and lay lower in the pelvis than usual. A small-bowel enema, done to check on the previous findings, failed to show any abnormality.

The patient continued to have occasional attacks of crampy periumbilical pain and nausea. Another flat plate taken during one of the attacks showed several dilated loops of gas-filled small bowel, with only a small amount of air in the colon.

On the seventh hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR. GRANTLEY W. TAYLOR: May we start off by seeing the x-ray films?

DR. RICHARD SCHATZKI: This is a postoperative film following lobectomy. It shows what was described in the report. These are the films of the gastrointestinal series. The report as stated in the record gives an erroneous impression regarding the permanency of the unusual finding in the small intestine. It was actually seen on only one film. The small intestine is widened locally, and its appearance suggests intussusception. The bowel proximal to it is widened, whereas on the earlier and later films taken on the same day there is no evidence of any abnormality, not even widening of the small intestine. These are the films taken at the time of

the small-bowel enema, the lower jejunum was studied particularly carefully, but no abnormality of any kind was seen. The bowel did not appear dilated. Additional films were taken at half-hour intervals over a period of one and a half hours, and again nothing abnormal was seen. A flat film taken on the next day showed definitely dilated loops of small intestine.

DR TAYLOR Dr Schatzki started by showing you the films of the chest, but I shall pass over the lung condition with only a brief comment. It is unfortunate that he developed pleurisy and lung abscesses and had to have an operation, but I cannot see any possible connection between the lung condition and the gastrointestinal tract.

Essentially, we have a patient with recurrent bouts of obstructing pain and vomiting occurring intermittently over a period of years. At the time of his second admission he was described as being a well developed, well nourished man in no acute distress, with slight tenderness in the lower abdomen but no other positive findings. These pains were characterized, at various times, by periumbilical cramps, which were almost invariably associated with vomiting and nausea. At times these attacks recurred at frequent intervals for as long as ten days, but at other times there were periods of remission, when the patient was absolutely free from discomfort and inconvenience, gained weight and was asymptomatic. To me, that type of crampy periumbilical pain, associated with vomiting, is indicative of partial intermittent intestinal obstruction, presumably of the small intestine. The vomiting started fairly promptly after the onset of the pain, and the symptoms eventually passed off by themselves. So we might say that whatever was causing this condition had abated spontaneously at the time of admission. There is nothing in the chart or the recorded appearance to suggest that he had an inflammatory process, such as appendicitis or acute cholecystitis.

The laboratory findings, including the temperature, were strikingly negative. He had a lot of x-ray studies at various times, all of which tended to exempt from suspicion the biliary tree and everything else but the intestinal tract. So we come to the problem of what was causing these intermittent bouts of intestinal obstruction, they appear to have been on a mechanical basis, without impairment of the circulatory state of the bowel. The only evidence that sheds any light on the nature of the process that was doing this is the x-ray observation that Dr Schatzki has just pointed out. What sort of things do leave a man in good health, with no abnormal laboratory findings, with intermittent bouts of certainly distorted bowel but without actual obstruction of the bowel? We always have abnormal bands and kinks and that sort of thing to consider. Since there had been no previous operation, artificially made adhesions could not have caused these

attacks. There is no description of a hernia. Of course, internal hernias are not infrequent, but they do not repeatedly resolve themselves in this fashion without active therapeutic intervention. Meckel's diverticulum is often associated with this type of symptomatology, but there is nothing in the protocol that justifies making the assumption that that condition was present. So we come to the problem of the x-ray condition, whatever it is, as an explanation of his symptomatology. The x-ray people are certainly "handing it to us on a platter" when they say, "There was a peculiar widening and crowding of the mucosal markings in the jejunum that was somewhat suggestive of an intussusception led by a small tumor mass." Even without such a gratuitous offering I think that we might arrive at the conclusion that some such condition was present. Certainly if we entertain the idea of tumor it seems to me that the condition of the patient in relation to the duration of symptoms argues against the presence of malignant neoplasm. When it comes to deciding what sort of benign neoplasm was involved, a histologic examination is required. There are leiomyomas, fibromas, lipomas and other rarer tumors of the small intestine. Someone will say, "What about lymphoblastoma?" That often behaves like a benign tumor in its leisurely progress, with freedom from hemorrhage and cachexia for some time, but after two years' duration there should have been evidence of lymphoblastoma elsewhere.

I cannot do more, Dr Mallory, than to say I believe that this patient had a primary neoplasm of the small intestine, probably benign, the histologic character of which I leave to you. He may have had a dyskinesia that justified the diagnosis of intussusception. Certainly, if he had an intussusception, it resolved itself without gross blood or pronounced clots in the stools, both of which are traditions in intussusception.

DR TRACY B MALLORY Dr Herrera, will you describe what was seen when the abdomen was first opened?

DR RODOLFO E HERRERA We operated because we were convinced that he had had repeated episodes of small-bowel obstruction. When we opened the abdomen, we found throughout the mesentery and omentum innumerable small pale-yellow granules, some of the nodes of the mesentery, in fact most of them, were enlarged and felt soft. In only one region — the midjejunum — was there any invasion of the small bowel. This area somewhat resembled regional enteritis, with thickening of the mesentery and invasion of the bowel wall causing almost complete obstruction. There was great disparity between the size of bowel proximal and distal to this loop. Because of the extent of the process in the mesentery we did not believe that we could cure him, and we entertained the diagnosis of lymphoma or tuberculosis at that time. To establish the diag-

osis conclusively and also since the region of the jejunum seemed to be irreversibly obstructed, we resected the jejunum and did a side-to-side enter-enterostomy

DR. MALLORY Would you care to add anything at this point, Dr Taylor?

DR. TAYLOR Not a thing The case is very instructive.

### CLINICAL DIAGNOSES

Recurrent intestinal obstruction

Granuloma, small bowel

### DR. TAYLOR'S DIAGNOSIS

Benign tumor of jejunum

### ANATOMICAL DIAGNOSIS

Malignant lymphoma (giant-follicle type) of jejunum, mesentery and omentum

### PATHOLOGICAL DISCUSSION

DR. MALLORY The pathologist was called in consultation in the midst of the operation The first specimen was a piece of the omentum, and frozen sections showed a picture that I never happen to have seen before—many isolated lymphoid follicles, all of which were quite separate from one another We thought at the time that it was a lymphoma of the so-called "giant-follicle type," although we had never seen a manifestation quite like this. When the resected specimen was brought over to the laboratory, a tumor mass was found, as Dr Herrera has told you, in the small bowel and the adjacent mesentery Sections of that showed obvious and typical lesions of giant-follicle lymphoma As perhaps you know, of all the types of lymphoma this is the one that ordinarily runs a relatively benign course. A duration of two years without generalized cachexia is not impossible with this type of lesion I think that it is fair to assume that this is what he had from the start of his intestinal symptoms I doubt that it can be tied in in any way with the chest disease

DR. SCHATZKI After we knew the cause of the patient's trouble, we went back over the films to see if we could find any evidence of the disease I could see what appeared to be a tumor on only one film, which was taken at the time the mass had intussuscepted and had produced obstruction When you know that there is something, it is rather discouraging to look carefully for it and still be unable to demonstrate it

DR. MALLORY This man, of course, will get x-ray treatment, and the prognosis is relatively good The average duration of this type of disease is nearly five years from the onset of symptoms, and he might easily live a number of years in an excellent state of health We believe, in this hospital, that when there is a lymphomatous involvement of a hollow viscus it is wise to resect it before initiating x-ray

treatment There is significant danger of spontaneous perforation of the lesion if x-ray treatment is started too vigorously when the intestinal tract is involved Do you agree, Dr Schatzki?

DR. SCHATZKI We have become more courageous but still advocate surgery if it can be done A single lesion probably offers the best prognosis

DR. HERRERA I should like to ask Dr Schatzki whether he thinks that the diagnosis might have been established if, instead of doing a small-bowel series in the usual way, they had allowed the Miller-Abbott tube to advance and had introduced barium through it

DR. SCHATZKI That would have offered a good chance, unless the Miller-Abbott tube had gone through the area of narrowing

DR. HERRERA I do not believe that it could have gone through

### CASE 32212

#### PRESENTATION OF CASE

A sixty-five-year-old Italian mother of ten children entered the hospital because of abdominal pain, nausea and vomiting

The patient had been in good health until one year prior to entry, when she began to complain of mild upper abdominal discomfort coming on usually in the evening and after meals There was no vomiting, diarrhea, chills or jaundice Ten days before entry, following a supper of ice cream and pie, the patient complained during the night of nausea and slight pain in the right lower quadrant, which became generalized by the following morning She also began to vomit and pass profuse watery stools After taking some pills prescribed by her local physician, the symptoms abated somewhat but the pain and vomiting of everything taken orally continued until admission

Physical examination showed a well developed and well nourished woman in no acute distress The tongue was dry and reddened The chest was clear except for a few transient rales at the right base The abdomen was evenly protuberant, soft and non-tender Peristalsis was active No masses were felt

The blood pressure was 198 systolic, 108 diastolic The temperature, pulse and respirations were normal

Examination of the blood showed a white-cell count of 12,700, with 82 per cent neutrophils The hemoglobin was 14 gm per 100 cc The serum bilirubin was 0.85 mg per 100 cc direct, and 1.0 mg indirect The total protein was 5.4 gm, per 100 cc, with an albumin-globulin ratio of 2.5 The chloride was 101 miliequiv per liter, and the nonprotein nitrogen 16 mg per 100 cc A blood Hinton test was negative The urine was normal A stool was guaiac negative

X-ray examination of the chest showed considerable increase in the markings throughout the lung fields, with a few nodular areas well out toward the periphery. The heart was within normal limits, and the aorta was tortuous. A plain abdominal film showed multiple dilated loops of small bowel and a large amount of gas and fluid in the cecum, ascending and transverse colon. A barium enema showed barium passing readily into the large bowel and into the region of the cecum. No defects were noted, but the preparation of the patient was not satisfactory. The barium was poorly evacuated. Multiple irregular faceted areas of calcification having the typical appearance of gallstones were found in the right upper quadrant. A Graham test showed rather poor concentration of the dye, but the gall bladder contracted fairly well after a fat-containing meal.

A Miller-Abbott tube was passed, which resulted in gradual decompression and improvement in the patient's condition. On the third hospital day a flat film showed the tip of the tube well down in the pelvis. There were still several loops of dilated small bowel. On the sixth hospital day another flat film of the abdomen showed a suggestion of a filling defect at the hepatic flexure of the colon, with dilatation of the cecum and ascending colon up to that point. A large gas bubble seemed to be in or near the gall bladder.

On the twelfth hospital day another barium enema was administered. The barium met a complete obstruction in the ascending colon close to the hepatic flexure. Fluoroscopically it was thought that the upper margin of the obstruction was shelf-like, but not enough barium passed the point to be certain of the type of lesion.

An intravenous pyelogram performed on the thirteenth hospital day revealed normally functioning kidneys and a soft-tissue pelvic mass, which appeared to be somewhat lobulated and compressed the bladder.

On the fourteenth hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR LAMAR SOUTTER. This woman came in with a story that sounds like intestinal obstruction. At the time of her operation, twelve days after entry, x-ray studies were again indicative of obstruction. Let us look first at the x-ray films.

DR RICHARD SCHATZKI. Unfortunately the first film of the chest and the films of the first barium enema are not available. I was told by the man who examined the patient at the time of the first barium enema that the examination was unsatisfactory owing to a large amount of fecal material.

These are the two flat films with the Miller-Abbott tube in place, the retained barium is mainly

in the transverse colon, the region of the ascending colon being filled with air. The Miller-Abbott tube had passed through the small intestine and is apparently just trying to negotiate the ileocecal valve, possibly it has already passed through the valve. This is the film taken at the time of the second barium enema, and you can see the obstruction just proximal to the hepatic flexure in the upper ascending colon. The obstruction is complete, no barium passes beyond the point of obstruction. Here you see the gallstones. The intravenous pyelogram may be of interest because it shows a soft-tissue mass that is pushing the bladder downward.

DR SOUTTER. When we go back over the history we find that the patient had been in good health until a year before entry, when she began to complain of mild upper abdominal discomfort coming on usually in the evening after meals. Upper abdominal discomfort, of course, does not give us much information. It is compatible with gallstones and chronic cholecystitis, which she has. On the other hand, the symptoms at that time were vague and could have been caused by many things. Can the entire story be explained on the basis of an inflamed gall bladder that was obstructing the ascending colon and the small bowel? In the first place, the acute onset of her disease, ten days before entry, does not lead one to believe that it was due to gall bladder trouble. There was not the typical pain with radiation to the back. She had profuse watery stools and a lot of vomiting, but little evidence of inflammation. She had only a slightly elevated white-cell count, and there was no fever, no tenderness, and no mass. Furthermore, the Graham test done a few days after entry showed that the gall bladder did not fill well, which is compatible with chronic cholecystitis and cholelithiasis, but it emptied well, which is incompatible with an acutely inflamed gall bladder. Therefore, we can say that at the time she came in the symptoms were probably not related to the gall bladder.

Could she have an intrinsic lesion in the colon that was causing obstruction but was relieved only to recur again in the hospital? She had no anemia. The serum protein was slightly depleted, with a normal albumin-globulin ratio, but the protein can be depleted in a person who has been vomiting for ten days and who has had profuse watery stools. The watery stools suggest that, if she had obstruction, it was not complete. Subacute obstruction will often give diarrhea. It is therefore possible that she came in with a lesion of the ascending colon at the hepatic flexure or just below it that was causing obstruction, which was relieved during the stay in the hospital. Why did that not show up at the time of the first barium enema? As Dr Schatzki has told us, this was an unsatisfactory procedure, owing to a lot of gas and feces, and the growth that could have caused temporary obstruction would not necessarily have been visualized at that time.



Why did the bowel not empty promptly after the barium enema? That is readily explained on the basis of irritation to the bowel from previous obstruction, so that at the time of entry she had ileus, paralytic in nature, secondary to obstruction. In other words, although the obstruction was temporarily relieved, as shown by the fact that the barium passed into the cecum at the time of the first barium enema, the bowel did not empty because it had not regained its tone.

Could she have had an extrinsic inflammatory lesion that subsequently obstructed the bowel? There again the hospital course is against it. It is possible that she had an acute cholecystitis following the cholecystogram. Occasionally an acute gall bladder becomes adherent to the omentum and so forth and obstructs the colon because of inflammatory adhesions. We do not know enough about the hospital course to say whether an inflammatory process was going on. It is not suggestive, however, and I shall therefore presume that it did not occur. We have no lead that she had difficulty with the right kidney. Since she had a normal pyelogram, it is likely that no renal tumor was pressing on the colon. The history is not particularly suggestive of an ulcer of the duodenum that had perforated, thus producing this obstruction.

Could she have had a lesion a little higher up in the intestines? If she had an obstruction before entry, which is probable, it could well have been a small-bowel obstruction that was not complete. What could have given a partial obstruction in the small bowel that was later relieved? This could have been caused by some growth at the ileocecal valve, probably one that projected or pressed into the lumen of the bowel and produced partial obstruction, with subsequent relief when it came out of the lumen. Along that line we think of such things as adenoma, leiomyoma, lipoma and so forth. There could well have been a certain amount of gas and feces in the cecum from paralytic ileus if the obstruction was above this level. We do not know why the second barium enema was given. It was apparently done because the patient again had obstructive symptoms. The fact that the barium failed to pass beyond the hepatic flexure, with a *fleck* of barium projecting out there, is suggestive that this was due to a growth at that level with complete obstruction, but she could also have had a growth at the ileocecal valve with intussusception up to the level of the hepatic flexure, so that the barium failed to go farther. Against intussusception is the fact that the stool was guaiac negative. Intussusception, however, is fairly rare in adults, particularly women, and it is nearly always associated with blood in the stool. We do not know whether she had blood in the stool at the time of the second enema, but she could perfectly well have had a small-bowel lesion that had intussuscepted

into the colon because it lay close to the ileocecal valve.

The intravenous pyelogram is interesting. The most frequent cause of a fairly well outlined pelvic mass pressing into the bladder in a woman who has passed the menopause with no particular story of pelvic difficulty is a fibroid uterus. It is difficult to visualize any obstructive lesion of the descending colon that would interfere with the bladder without there being a definite palpable mass. Furthermore, without signs of obstruction at that level at the time of the two barium enemas, the lesion appears to have been higher. Further suggestive evidence of a lesion in the small bowel, rather than one in the large bowel, is the fact that the vomiting came on almost immediately. With a polypoid type of growth obstructing the small bowel, one would expect vomiting earlier than if she had had obstruction at the hepatic flexure.

In conclusion I shall say that this woman's lesion was neoplastic, that it was probably benign, because of the blood picture and history, that she had temporary obstruction prior to coming in, which was relieved on entry, that the lesion was probably in the region of the ileocecal valve and that she had intussusception at the time that the second barium enema was taken. It is, of course, impossible to exclude a neoplastic lesion at or just below the hepatic flexure.

DR. SCHATZKI: Against intussusception is perhaps the fact that in the film you can see air in what appears to be a normal cecum.

#### CLINICAL DIAGNOSES

Cholelithiasis?  
Carcinoma of large bowel

#### DR. SOUTTER'S DIAGNOSIS

Benign tumor of ileocecal valve, with intussusception of ileum into cecum and ascending colon

#### ANATOMICAL DIAGNOSIS

Adenocarcinoma of ascending colon

#### PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: This patient was operated on by Dr. Langdon Parsons. I am sorry that he is not here to describe the operative findings. He found a tumor in the ascending colon, and resected it, together with a small portion of the terminal ileum. The specimen that we received showed a carcinoma of the ascending colon at about its mid-portion, it was 5 or 6 cm. from the ileocecal valve and 13 cm. from the edge of the resection. There were a few enlarged lymph nodes in the attached mesentery, but these were histologically free from metastases. If an intussusception had been present, there was no trace of it at the time of operation.

X-ray examination of the chest showed considerable increase in the markings throughout the lung fields, with a few nodular areas well out toward the periphery. The heart was within normal limits, and the aorta was tortuous. A plain abdominal film showed multiple dilated loops of small bowel and a large amount of gas and fluid in the cecum, ascending and transverse colon. A barium enema showed barium passing readily into the large bowel and into the region of the cecum. No defects were noted, but the preparation of the patient was not satisfactory. The barium was poorly evacuated. Multiple irregular faceted areas of calcification having the typical appearance of gallstones were found in the right upper quadrant. A Graham test showed rather poor concentration of the dye, but the gall bladder contracted fairly well after a fat-containing meal.

A Miller-Abbott tube was passed, which resulted in gradual decompression and improvement in the patient's condition. On the third hospital day a flat film showed the tip of the tube well down in the pelvis. There were still several loops of dilated small bowel. On the sixth hospital day another flat film of the abdomen showed a suggestion of a filling defect at the hepatic flexure of the colon, with dilatation of the cecum and ascending colon up to that point. A large gas bubble seemed to be in or near the gall bladder.

On the twelfth hospital day another barium enema was administered. The barium met a complete obstruction in the ascending colon close to the hepatic flexure. Fluoroscopically it was thought that the upper margin of the obstruction was shelf-like, but not enough barium passed the point to be certain of the type of lesion.

An intravenous pyelogram performed on the thirteenth hospital day revealed normally functioning kidneys and a soft-tissue pelvic mass, which appeared to be somewhat lobulated and compressed the bladder.

On the fourteenth hospital day an operation was performed.

#### DIFFERENTIAL DIAGNOSIS

DR LAMAR SOUTTER. This woman came in with a story that sounds like intestinal obstruction. At the time of her operation, twelve days after entry, x-ray studies were again indicative of obstruction. Let us look first at the x-ray films.

DR RICHARD SCHATZKI. Unfortunately the first film of the chest and the films of the first barium enema are not available. I was told by the man who examined the patient at the time of the first barium enema that the examination was unsatisfactory owing to a large amount of fecal material.

These are the two flat films with the Miller-Abbott tube in place, the retained barium is mainly

in the transverse colon, the region of the ascending colon being filled with air. The Miller-Abbott tube had passed through the small intestine and is apparently just trying to negotiate the ileocecal valve, possibly it has already passed through the valve. This is the film taken at the time of the second barium enema, and you can see the obstruction just proximal to the hepatic flexure in the upper ascending colon. The obstruction is complete, no barium passes beyond the point of obstruction. Here you see the gallstones. The intravenous pyelogram may be of interest because it shows a soft-tissue mass that is pushing the bladder downward.

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staphylococcal infections in human beings in which relapses have occurred because of localized infections, penicillin therapy has often been continued for long periods without the development of any measurable degree of penicillin resistance. Although it is too soon to draw any conclusions on this point, the evidence so far available suggests that, except for staphylococcal infections, penicillin resistance will probably not be of any great clinical importance.

The absorption and excretion of penicillin and its diffusion into various body fluids are the next important features to be considered. After intramuscular injections, absorption of penicillin is rapid, the maximum level being achieved within fifteen to twenty minutes. Thus, it is entirely unnecessary and superfluous to begin

therapy with a single intravenous dose, as many physicians are inclined to do. After the drug is absorbed, it is rapidly eliminated, so that 80 per cent of the intramuscular dose appears in the urine within the first two hours, and less than 5 per cent remains after four hours. The rapid absorption and rapid elimination of penicillin are therefore responsible for the greatest disadvantage of penicillin therapy at present, namely, the necessity for frequent parenteral injections. Of the many methods used in attempts to delay absorption, Rammelkamp and Kirby consider the intramuscular injection of penicillin in beeswax-peanut oil mixtures to be the most promising. Effective blood levels can be maintained for as long as twenty-four hours after 300,000 units of penicillin given in 1 cc. of such a mixture.

Concerning oral preparations, these authors consider that none of the enteric coatings, oils or acids thus far employed give better results than those obtained with the ingestion of penicillin dissolved in tap water. With any of these preparations,

five or six times as much penicillin must be administered to produce levels equivalent to those obtained following parenteral injections. It is worth mentioning that even this ratio is valid only when the penicillin is given before meals, since in most persons little or no penicillin is absorbed if it is given orally within a short time after the ingestion of food.

The diffusion of penicillin into body fluids and cavities occurs irregularly and generally only to a small extent. For this reason, local therapy as well as parenteral treatment is usually necessary in the treatment of infections of the pleura, pericardium and joints. In some localized infections, such as well established empyemas, parenteral injections are unnecessary, favorable results often being obtained by local injections alone. In meningitis, al-

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In certain conditions, notably subacute bacterial endocarditis, various forms of late syphilis and chronic osteomyelitis, the factor of penetration is extremely important. Favorable results can be obtained and relapses avoided only by the maintenance of high blood levels continuously for long periods.

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## DOSAGE OF PENICILLIN

THERE is considerable confusion in the minds of most physicians about the dosage of penicillin in the treatment of various infections. This is due in part to the fact that the early studies on penicillin therapy were made when the material was quite scarce, as a result of which attempts were made to define the dose in terms approximating the minimum effective amount. When the supply of the antibiotic became more plentiful, the trend was in the opposite direction, large doses being advocated and used empirically. Some justification for the large doses was found in the better results achieved in such conditions as subacute bacterial endocarditis and other infections in which small doses had failed to produce a satisfactory clinical response. A

knowledge of the factors determining the optimum dose to be used in any given set of circumstances, however, is essential if one is to provide adequate therapy and at the same time to avoid ridiculous waste of large amounts of this valuable material.

The factors determining the dosage of penicillin in infections have been recently reviewed by Rammelkamp and Kirby\*. These authors point out that there is a closer correlation with penicillin than with sulfonamides between the sensitivity of bacteria in vitro and the clinical results obtained. This is attributed in part to the fact that sulfonamides are inhibited by substances contained in pus and exudates, whereas the same is not true of penicillin. Penicillin is selective in its activity. For the most part, this selectivity refers to the high degree of antibacterial action of penicillin against gram-positive bacteria and its failure to inhibit the growth of most gram-negative bacteria. There is considerable variation, however, in the degree of sensitivity of different bacteria and even of different strains of the same organism. For practical purposes, however, most of penicillin-sensitive bacteria that are frequently encountered, particularly the gonococcus, pneumococcus and beta-hemolytic streptococcus, exhibit variations that are not of sufficient clinical significance to affect the results of therapy. In cases of subacute bacterial endocarditis and in certain staphylococcal infections, on the other hand, there may be wide variations in the sensitivity of the etiologic organisms. It is only in the latter types of cases, therefore, that a knowledge of the sensitivity of the organism may be of importance both from the standpoint of therapy and that of prognosis.

The problem of acquired resistance or fastness of bacteria has received intensive study because of the importance of that feature in relation to sulfonamide therapy. It has been shown that most of the penicillin-susceptible organisms develop resistance only after prolonged exposure to the antibiotic. Clinical experience has indicated that, with the exception of the staphylococcus, well substantiated instances of penicillin resistance acquired during therapy have been rare. Furthermore, in certain cases of streptococcal, pneumococcal and

\*Rammelkamp, C. H., and Kirby, W. M. M. Factors determining dosage of penicillin in treatment of infections. *Bull. New York Acad. Med.* 21: 656-672, 1945.

staphylococcal infections in human beings in which relapses have occurred because of localized infections, penicillin therapy has often been continued for long periods without the development of any measurable degree of penicillin resistance. Although it is too soon to draw any conclusions on this point, the evidence so far available suggests that, except for staphylococcal infections, penicillin resistance will probably not be of any great clinical importance.

The absorption and excretion of penicillin and its diffusion into various body fluids are the next important features to be considered. After intramuscular injections, absorption of penicillin is rapid, the maximum level being achieved within fifteen to twenty minutes. Thus, it is entirely unnecessary and superfluous to begin

therapy with a single intravenous dose, as many physicians are inclined to do. After the drug is absorbed, it is rapidly eliminated, so that 80 per cent of the intramuscular dose appears in the urine within the first two hours, and less than 5 per cent remains after four hours. The rapid absorption and rapid elimination of penicillin are therefore responsible for the greatest disadvantage of penicillin therapy at present, namely, the necessity for frequent parenteral injections. Of the many methods used in attempts to delay absorption, Rammelkamp and Kirby consider the intramuscular injection of penicillin in beeswax-peanut oil mixtures to be the most promising. Effective blood levels can be maintained for as long as twenty-four hours after 300,000 units of penicillin given in 1 cc of such a mixture.

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In certain conditions, notably subacute bacterial endocarditis, various forms of late syphilis and chronic osteomyelitis, the factor of penetration is extremely important. Favorable results can be obtained and relapses avoided only by the maintenance of high blood levels continuously for long periods.

Rammelkamp and Kirby also emphasize the fact that, although penicillin is highly effective against the organisms present in the throat in patients with tonsillitis and pharyngitis, lasting beneficial effects are exerted only when penicillin is given parenterally. Local therapy with gargles or sprays is ineffective. After intramuscular injections, however, streptococci disappear or rapidly diminish, but they reappear if treatment is discontinued too soon. It has been definitely demonstrated that, in order to obtain a permanent cure in cases of streptococcal sore throat, it is necessary to continue treatment for five or more days. In pneumococcal pneumonia, too, it is necessary to continue treatment for several days after apparent recovery to ensure sterilization of the infected tissues and to prevent relapse. It is possible that final recovery is brought about in these cases and in certain other infections with the help of the body's own defense mechanisms.

The frequency with which doses are given depends, of course, on the time during which effective levels must be maintained. Rammelkamp and Kirby present evidence that indicates that some antibacterial effect persists after the time when penicillin is no longer demonstrable in the serum by the usual tests. Doubling the size of the dose produces a blood level that is twice as high, but the effective level is prolonged by only one third. The high levels that result from the use of extremely large doses are usually well in excess of those necessary to exert the maximal antibacterial effect. Injections of 20,000 units produce levels in the blood that are considered to be maximum against the staphylococcus for less than one hour, although definite bacteriostasis probably persists for another two hours. For the hemolytic streptococcus, on the other hand, the same dose produces concentrations that have maximum antibacterial action for more than two and a half hours and partial inhibitory levels for another one and a half to two hours. Other factors of importance in determining the size of the dose of penicillin are the severity of the infection, the vascularity of the areas involved and the barriers through which penicillin must diffuse or penetrate to come in contact with the infecting organism.

On the basis of all these factors it is possible to plan rational schemes of treatment. In staphylococcal infections, for example, 25,000 units every two hours will provide optimal levels continuously in the blood stream, for streptococcal infections, 15,000 units every three hours are adequate for this purpose. Two points are especially emphasized. One is that doses producing optimal concentrations of penicillin in the blood stream are all that are necessary. Although larger doses raise the concentration of penicillin, they do not increase the already maximum antibacterial activity and are therefore wasteful. The other point is that, for all practical purposes, penicillin remains active in the tissues for only three, or at most four, hours after the usual therapeutic dose. The use of penicillin at intervals longer than four hours is therefore potentially dangerous, even though occasional infections due to highly sensitive bacteria may respond favorably to doses given at wider intervals.

## EFFECT OF VITAMIN SUPPLEMENTS

Our British cousins, a little less enthusiastic than ourselves, who are a mixture of various races although speaking a similar tongue, seem inclined to take their vitamins with a grain of salt. It is not that they are any less serious about them, it is rather that, conservatively, they seem to prefer them from an apothecary's shop than a slot machine and are even inclined to doubt that health improves in direct proportion to the amount of vitamin concentrate assimilated.

As recently as February, 1946, Bransby, Burns, Magee and MacKecknie\* published the results of a study on the effect of a daily vitamin supplement on the health and development of children. The test was made on 1620 children, aged five to fourteen years, attending day schools in the towns of Stoke-on-Trent and Salford. The subjects were divided into the conventional two groups at random, one of which received a daily placebo and the other a capsule containing 4000 int units of vitamin A, 1 mg of vitamin B<sub>1</sub>, 2 mg of riboflavin, 20 mg of nicotinamide, 50 mg of ascorbic acid and 600 int units of

\*Bransby, E. R., Burns, J. L., Magee, H. E., and MacKecknie, D. M. Effect of daily vitamin supplement on health and development of children. *Brit. M. J.* 1:193-197, 1946.

vitamin D. The tests, which ran for a year, were similar in the two towns but not identical. In Stoke medical, dental and anthropometric data were collected three times during the year, and in Salford twice, in Salford facts were gathered on the economic condition of the subjects, in Stoke dynamometer and hanging-bar tests were performed, and in Salford hearing was tested by means of the audiometer.

The results were essentially nil—a temporary disappointment, no doubt, to the vitamin enthusiasts and faddists: the vitamin supplement had no apparent consistent effect “on growth, strength, endurance, fatigue potential, incidence or severity of clinical conditions, hearing and absenteeism from school. The vitamin supplement had a beneficial effect on gingivitis in Stoke but not in Salford.”

These British experiments, it is true, did not elaborate on all the developmental, nutritional and clinical factors that could have been affected by vitamin therapy, nor did they attempt to measure the incalculable *joie de vivre* that might have resulted from such regular indulgence in these encapsulated cocktails, or to initiate any manner of “shock therapy” by the use of massive doses, such as has been done effectively for certain particular purposes. On the basis of their findings, however, the authors suggest that the recommended vitamin requirements of the National Research Council of the United States are too high, with particular reference to ascorbic acid, that the amounts contained in the average diet are sufficient for the maintenance of satisfactory health and that, consequently, the need for supplemental rations has been exaggerated. These results, however, are only suggestive. We must continue to remember that there is a great deal more to normal nutrition than an adequate vitamin intake and that, contrary to a growing popular belief, supplementary vitamins do not constitute a complete, concentrated diet.

## MASSACHUSETTS MEDICAL SOCIETY

### EXECUTIVE COMMITTEE OF THE COUNCIL

On April 24, 1946, the Executive Committee of the Council, on the recommendation of the Committee on Membership and representatives from the supervising centers, took the following actions:

Allowed the following named fellows, applying for retirement and with all dues paid and in good standing, to retire under the provisions of Chapter I, Section 5, of the by-laws:

Bartlett, William B. (Middlesex South), 28 Monument Street, Concord  
Beals, Lester H. (Franklin), 701 Plymouth Road, Claremont, California  
Bigelow, Enos H. (Middlesex South), 65 Edgell Road, Framingham Centre  
Boutwell, Horace K. (Norfolk), 15 Green Street, Brookline  
Bremer, J. L. (Suffolk), 113 Marlboro Street, Boston  
Canavan, Myrtelle M. (Norfolk), 2061 Dorchester Avenue, Boston  
Draper, Alexis L. (Norfolk), 1107 Washington Street, Dorchester Centre  
Duckering, Florence W. (Suffolk), 483 Beacon Street, Boston  
Grant, Justin F. (Suffolk), 587 Tremont Street, Boston  
Higgins, George V. (Norfolk South), Corner Main and Warren streets, Randolph  
Hollister, F. M. (Plymouth), South Duxbury  
Holt, William L. (Hampshire), Amherst  
Merrett, S. Virgil (Bristol South), 297 Osborn Street, Fall River  
Page, Calvin G. (Suffolk), 128 Marlboro Street, Boston  
Phelps, John S. (Essex South), 768 Boston Street, Lynn  
Schirmer, J. Walter (Suffolk), 85 Lawton Road, Needham  
Tilden, Irving N. (Bristol South), Mattapoisett  
Tyler, Winsor M. (Middlesex South), 1482 Commonwealth Avenue, Brighton

Allowed the following named fellow, applying for retirement but who is in arrears of dues for the year 1945, to have his dues for the year 1945 to the Massachusetts Medical Society remitted under the provisions of the by-laws, Chapter I, Section 6, and then to retire under the provisions of Chapter I, Section 5, of the by-laws:

Walsh, John E. (Suffolk), 238 Beach Street, Revere

Allowed the following named fellows, applying for resignation with all dues paid and in good standing, to resign under the provisions of Chapter I, Section 7, of the by-laws:

Adler, Alexandra (Suffolk), Duke University, Durham, North Carolina  
Finnegan, William F. (Non-Resident), 380 North Eighth Street, Lebanon, Pennsylvania  
Haskell, C. D. (Non-Resident), 141 S. Meridian Street, Indianapolis, Indiana  
Hyde, Fritz C. (Non-Resident), 320 East 72nd Street, New York City  
Joy, Genevieve L. (Non-Resident), 202 South Palouse Street, Walla Walla, Washington  
Leone, Joseph P. (Norfolk South), Quincy City Hospital, Quincy  
McMackin, John V. (Non-Resident), 406 Huntington Building, Miami, Florida  
Redlich, Frederick C. (Non-Resident), 333 Cedar Street, New Haven, Connecticut  
Staples, O. Sherwin (Norfolk), Hitchcock Clinic, Hanover, New Hampshire  
Yahn, George W., III (Suffolk), P. O. Box 38, Camarillo, California

Allowed the following named fellows, applying for resignation from the Massachusetts Medical Society but who are in arrears of dues, to have these dues owed the Massachusetts Medical Society remitted under Chapter I, Section 6, of the by-laws and then to resign from the Massachusetts Medical Society under the provisions of Chapter I, Section 7, of the by-laws:

Forster, Francis M. (Norfolk), 1025 Walnut Street, Philadelphia, Pennsylvania  
Ruesch, Jurgen (Middlesex South), University of California Medical School, The Medical Center, San Francisco, California

Allowed the following named fellows to change their membership from one district society to another, without change of legal residence, under the provisions of Chapter III, Section 3, of the by-laws:

Bayles, Theodore B, 94 Summer Street, Weston (Middlesex South to Suffolk)  
 D'Errico, Emilio, 14 Everett Avenue, Winchester (Remain in Middlesex South)  
 Hanson, Wm T, 30 Bellevue Road, Stoneham (Remain in Plymouth)  
 Hare, Hugh F, 66 Fountain Street, West Newton (Middlesex South to Suffolk)  
 Newell, John L, 35 Walnut Place, Brookline (Norfolk to Suffolk)  
 Shain, Arthur I, 63 Bay State Road, Boston (Suffolk to Norfolk)  
 Thorn, George W, 983 Memorial Drive, Cambridge (Middlesex South to Suffolk)  
 Warren, Richard, 30 Heath Street, Brookline (Remain in Suffolk)

had been a member of the staff of the Newton-Welles Hospital for twenty-six years. He was a fellow of the American Medical Association.  
 A son, four daughters and a sister survive.

McLEOD — Melvin S. McLeod, M.D., of Melrose, died February 26. He was in his fiftieth year.  
 Dr. McLeod received his degree from the University of Vermont College of Medicine in 1920.  
 His widow and two sons survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### PERSONNEL NOTES

William J. Welch, M.D., has been appointed physician in-chief of the Mobile Blood Donor Unit of the Division of Biologic Laboratories, Massachusetts Department of Public Health. Dr. Welch, who served for two years in the European Theater of Operations as a captain in the Army Medical Corps, has charge of the organization and technical operation of the field team that collects the voluntary blood donations.

Donald A. Martin, M.D., has been appointed director of the Massachusetts Hospital and Health-Center Survey Program. The survey was launched by Governor Tobin for the purpose of studying existing hospital and health facilities in anticipation of passage of the Hill-Burton Bill (S 191). Prior to his appointment, Dr. Martin was acting superintendent of the Lakeville State Sanatorium in Middleboro.

Robert E. Ober, M.D., epidemiologist with the Division of Communicable Diseases, Massachusetts Department of Public Health, has returned to duty following twenty-nine months overseas service with the Mediterranean Allied Air Forces.

Robert A. MacCready, M.D., recently discharged from the Army Medical Corps, where he held the rank of major, has returned to the Massachusetts Department of Public Health as epidemiologist in the Division of Communicable Diseases. He will be in administrative charge of the Laboratory Approval Program.

Mary Carr Baker, formerly supervisor of public-health education, Massachusetts Department of Public Health, is now field program supervisor of the new Blood Program. A field representative, Mrs. Baker supervises collaborative activities between the Department, the American Red Cross and community organizations in arranging for local participation in the Blood Donor Service.

Philip W. Johnston, Ph.D., has returned to the Division of Maternal and Child Health as research consultant in Field Service in Child Growth and Development, his duties including the preparation and validation of tests of vision and hearing for school children. During the war, Dr. Johnston held the rank of lieutenant in the United States Naval Reserve. He was first attached to the Bureau of Naval Personnel as a psychologist but later spent eighteen months in the Pacific area as radar officer on the U.S.S. *Boston*.

Leon A. Alley, M.D., has returned from duty in the European Theater of Operations as a lieutenant colonel after having served five years in the Army Medical Corps. He will resume his position as superintendent of the Lakeville State Sanatorium in Middleboro.

Elizabeth E. Barry, R.N., B.N., has been appointed supervising instructor in public-health nursing (pediatrics), Bureau of Public Health Nursing for the Rheumatic Fever Program, which is soon to be established in the Massachusetts Department of Public Health. She is a graduate of Yale University School of Nursing and Massachusetts State College.

Jane Y. Harshberger, R.N., M.A., a graduate of Yale University School of Nursing and of the University of Pennsylvania, has recently joined the staff of the Bureau of Public Health Nursing as supervising instructor in public-health nursing. She is conducting an educational program in maternity nursing for public-health and hospital nurses.

Reinstated the following named physicians, who have been deprived of membership for the nonpayment of dues, provided their arrears in dues at the time of deprivation both to the Massachusetts Medical Society and to their district societies, plus current year dues both to the Massachusetts Medical Society and to their district societies be sent to the Treasurer of the Society, in accordance with Chapter I, Section 10, of the by-laws:

Bennett, Max (Bristol North), 176 County Street, Attleboro  
 Gilbert, Meyer M. (Worcester), 30-A Boynton Street, Worcester  
 McDonald, J. F. (Worcester North), Main Street, Ashburnham  
 O'Brien, John Francis (Middlesex North), 77 Payson Road, Brookline  
 Tynan, J. P. (Suffolk), 801 Broadway, South Boston

Allowed the following named fellows, who have been ill for a number of years and totally disabled or who have been totally disabled through military service, to have their dues to the Massachusetts Medical Society remitted in the future as long as they are permanently disabled and unable to carry on medical practice and duties under the provisions of Chapter I, Section 6, of the by-laws:

Champ, Anthony M. (Plymouth), 109 Manomet Street, Brockton  
 Hendry, John J. (Suffolk), 681 Mountain Avenue, Revere  
 Krieger, William L. (Norfolk South), 15 Lincoln Avenue, Wollaston  
 Sawyer, Alpha R. (Norfolk), 79 Poplar Street, Roslindale  
 Sweeney, William J. (Middlesex East), 4 Avon Street, Wakefield

Allowed the following named fellow, who was deprived of membership in the Massachusetts Medical Society in 1942 on recommendation of the Committee on Membership to the Executive Committee, to be restored to active membership in good standing under the provisions of Chapter I, Section 10 of the by-laws. Former deprivation of fellowship was recommended because of nonpayment of dues. No information was obtained that he was in active military service:

Quigley, Thomas J. (Suffolk), 1633 Tremont Street, Boston

The personnel of the Committee on Membership is as follows: Harlan F. Newton, *chairman*, Roy V. Baketel, William A. R. Chapin, Peirce H. Leavitt, and Samuel N. Vose. The representatives of the supervising censors were as follows: William H. Allen, H. Quimby Gallupe, and Albert E. Parkhurst.

MICHAEL A. TIGHE, M.D., *Secretary*  
Executive Committee

### DEATHS

JACK — Lewis H. Jack, M.D., of West Newton, died May 3. He was in his seventy-fourth year.

Dr. Jack received his degree from Harvard Medical School in 1899. At various times during his medical career he was associated with the Boston City, Boston Lying-in, Long Island, Waltham, Winchester and Cambridge hospitals. He



## MISCELLANY

## DEDICATION AT McLEAN HOSPITAL

On May 17, the Scientific Research Laboratory of the McLean Hospital at Waverley, a unit of the Massachusetts General Hospital, was dedicated. The morning program included talks by Dr C K Drinker and Dr Jordi Folch. Following luncheon and inspection of the laboratory, addresses were given by Dr Stanley Cobb, Dr Herbert S Gasser, of New York City, and Dr Wilder Penfield, of Montreal. At the reception and dinner, held at the Harvard Club that evening, Dr E A Strecker, of Philadelphia, was the principal speaker.

## BOOKS — WAR VICTIMS

During the war, the libraries of half the world were destroyed in the fires of battle and in the fires of hate and fanaticism. Where they were spared physical damage, they were impoverished by isolation. There is an urgent need — now — for the printed materials that are basic to the reconstruction of devastated areas and that can help to remove the intellectual blackout of Europe and the Orient.

There is need for a pooling of resources and for co-ordinated action in order that the devastated libraries of the world may be restocked, so far as possible, with needed American publications. The American Book Center for War Devastated Libraries, Incorporated, has come into being to meet this need. It is a program that is born of the combined interests of library and educational organizations, of governmental agencies and of many other official and nonofficial bodies in the United States.

The American Book Center is collecting and is shipping abroad scholarly books and periodicals that will be useful in research and necessary in the physical, economic, social and industrial rehabilitation and reconstruction of Europe and the Far East.

The Center cannot purchase books and periodicals, it must depend on gifts from individuals, institutions and organizations. Each state will be organized to participate in the program through the leadership of a state chairman. Other chairmen will organize interest in the principal subject fields.

Co-operation with these leaders or direct individual contributions are welcomed.

**What is needed** — Shipping facilities are precious and demand that all materials be carefully selected. Emphasis is placed on publications issued during the past decade, on scholarly books that are important contributions to their fields, on periodicals (even incomplete volumes) of significance and on fiction and nonfiction of distinction. All subjects — history, the social sciences, music, fine arts, literature and especially the sciences and technologies — are wanted.

**What is not needed** — Textbooks, out-dated monographs, recreational reading, books for children and young people, light fiction, materials of purely local interest, popular magazines, such as *Time*, *Life*, *National Geographic* and so forth, and popular nonfiction of little enduring significance, such as Gunther's *Inside Europe*, Haliburton's *Royal Road to Romance* and so forth, should not be sent. Only carefully selected federal and local documents are needed, and donors are requested to write directly to the Center with regard to specific documents.

**How to ship** — All shipments should be sent prepaid via the cheapest means of transportation to The American Book Center, c/o The Library of Congress, Washington 25, D C. Although the Center hopes that donors will assume the costs of transportation of their materials to Washington, when this is not possible, reimbursements will be made on notification by card or letter of the amount due. The Center cannot accept material that is sent collect. Reimbursement cannot be made for packing or other charges beyond actual transportation. When possible, periodicals should be tied together by volume. It will be helpful if missing issues are noted on incomplete volumes.

## CORRESPONDENCE

## SCARLET FEVER OR STREPTOCOCCAL INFECTION?

*To the Editor* Sing a dirge for scarlet fever — it will soon be as extinct (statistically) as the Dodo bird and the heath hen!

To be sure the quarantine period for the disease has been cut from six to three weeks in most places, but this three weeks out of a family's life, when a case of "streptococcus throat" (caused by the same strain of the same "bug") is not quarantined at all, is a useless sacrifice so far as controlling the spread of the disease is concerned. So why quarantine?

Despite the fact that recent advances have proved that we can, with the first few injections of penicillin, render the throat free from streptococci and practically prevent complications, the Blue Cross will only pay for hospitalization of its policyholders when they *have* complications! It will, however, pay without question for hospitalization of "hemolytic streptococcus throats with a toxic rash" (If there is one disease in which hospitalization is advisable to save life and prevent permanent crippling, it is scarlet fever — *all* patients should be able to get injections of penicillin every three hours for *at least* six days.)

Henceforth, I see no cases of scarlet fever. All my patients will have streptococcus throats with toxic rashes. No more quarantine penalties, no more "gypping" by the Blue Cross of my patients! How about yours? Statistics will prove, I am sure, that in a few years there is no such thing as scarlet fever!

It is another version of the old story of diphtheria. With the advent of antitoxin in England, antivivisectionists pointed out, quite correctly, that there was a sharp increase in the number of cases of diphtheria. They failed to mention, however, that there were *no* cases of laryngeal croup. The profession had been educated to call diphtheria "diphtheria." Why not let us call streptococcal infections "streptococcal infections"?

PAUL R WITHINGTON, M D

350 Randolph Avenue  
Milton 86, Massachusetts

## DEPRIVATION OF LICENSE

*To the Editor* At the meeting of the Board of Registration in Medicine held May 8, the Board voted to suspend the registration of Dr Jean C Marchand, 210 Lafayette Street, Salem, for six months because of gross misconduct in the practice of his profession as shown by violation of the Federal Narcotic Act.

H QUIMBY GALLUPE, M D, Secretary

State House  
Boston

## REPORT OF MEETING

## MEDICAL LIBRARY ASSOCIATION

The Medical Library Association held its forty-fifth annual meeting in New Haven, Connecticut, on March 25, 26 and 27. Headquarters were at the Hotel Taft and sessions met in the Historical Library, Sterling Hall of Medicine, Yale University. The program featured reports on the Army Medical Library, a symposium entitled "International Co-operation" and addresses on the subjects "Training for Medical Librarianship" and "British Medical Libraries in Wartime."

The following officers were elected: president, Dr Walton B McDaniel, 2d, of the College of Physicians, Philadelphia, vice-president, Dr C Abbott Behing, of Newark, New Jersey, secretary, Miss Heath Babcock, of the New York State Medical Library, Albany, New York, and treasurer, Mr Jurgen G Raymond, of the New York Academy of Medicine, New York City.

It was voted to hold the 1947 convention in Cleveland, Ohio, the exact date to be determined later.

## EASTERN ASSOCIATION OF ELECTROENCEPHALOGRAPHERS

The second regular meeting of the Eastern Association of Electroencephalographers was held on Friday, April 12, at the Postgraduate Club of the Institute of Living at Hartford, Connecticut, with thirty-six members present. A constitution and by-laws were adopted, creating a new office of vice-chairman, to which post Dr Herbert H. Jasper, of the Neurological Institute of Montreal, was elected.

As chairman of the Liaison Committee, Dr Hallowell Davis reported that the American Physiological Society had appointed Dr Herbert H. Jasper and Dr Frederick A. Gibbs to represent their society on the joint committee to review the problems of clinical electroencephalography and to consider appropriate action to promote a high standard of electroencephalography. The Council on Physical Medicine of the American Medical Association has also replied favorably to the memorandum of the Eastern Association of Electroencephalographers, with the American Neurological Association and the American Psychiatric Association both informally expressing favorable interest.

Dr Milton H. Kibbe, of Springfield, Massachusetts, presented a paper describing experiences and findings in electroencephalography in an Army general hospital, with Dr Charles E. Henry following with a corresponding paper based on Navy experience.

At the meeting on Friday, March 1, at the Institute of Living at Hartford, Connecticut, when the Eastern Association of Electroencephalographers was organized, Dr Robert S. Schwab was elected chairman and Dr Charles W. Stephenson was elected recorder.

## NOTICES

### ANNOUNCEMENTS

Dr Louis Hermanson announces the removal of his office to 171 Bay State Road, Boston.

Dr John A. Murphy announces the opening of an office at 47 Bay State Road, Boston, for the practice of gynecology and obstetrics.

Dr Frederick P. Nadel, on termination of military service, is resuming the practice of medicine and surgery at 269 Harvard Street, Cambridge 39.

## NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, June 6, at 7 15 p.m., in the classroom of the Nurses' Residence. Dr Edwin B. Astwood will speak on the subject "Thiouracil in the Treatment of Hyperthyroidism." Dr Merry Pittman will be chairman.

## GRANTS AND FELLOWSHIPS IN CANCER RESEARCH

The Committee on Growth of the National Research Council, acting for the American Cancer Society, announces that it will entertain applications for grants in cancer research to become effective July 1, 1947. Applications will be received until September 15, 1946. Applications for fellowships and senior fellowships in cancer research of the American Cancer Society for the ensuing year will be received until December 1, 1946.

To date the Committee on Growth has recommended to the American Cancer Society a total of seventy-five research grants and fourteen fellowships. The committee will continue to recommend support of research in the basic sciences

and in clinical investigative medicine broadly pertaining to problems of growth. It will also continue to rely heavily for counsel on its advisory divisions of chemistry, biology, physics and clinical investigation and their subjacent panels in specialized areas of research.

Applications for research grants for the current year will no longer be entertained. Communications should be addressed to the Committee on Growth, Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

## NEW ENGLAND HEART ASSOCIATION

The annual meeting of the New England Heart Association will be held on Monday, June 3, in the Dowling Amphitheater of the Boston City Hospital at 8 15 p.m. The scientific program will be preceded by a short business meeting, including the election of officers for the ensuing year.

### PROGRAM

Indications for Removal of Foreign Bodies from the Heart, and the Technic of Cardiomy Dr Dwight E. Harken

Electrocardiographic Variations in Heart Trauma Dr Paul Zoll

### DISCUSSION

Interested physicians and medical students are invited to attend.

## SOCIETY MEETINGS AND CONFERENCES

### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, MAY 30

#### FRIDAY, MAY 31

\*9-00-10 00 a.m. The Role of Infection in Shock Dr Joseph C. Aub.  
Joseph H. Pratt Diagnostic Hospital  
\*10 00 a.m.-12 00 m. Medical Staff Rounds Peter Bent Brigham Hospital

#### MONDAY, JUNE 3

\*12 15-1 15 p.m. Clinicopathological Conference Peter Bent Brigham Hospital

#### TUESDAY, JUNE 4

\*12 15-1 15 p.m. Clinicoradiological Conference Peter Bent Brigham Hospital

#### WEDNESDAY, JUNE 5

\*10 30-11 30 a.m. Medical Clinic. Isolation Building Amphitheater Children's Hospital  
\*12-00 m. Clinicopathological Conference. (Children's Hospital) Amphitheater, Peter Bent Brigham Hospital  
\*2 30-4 00 p.m. Combined Clinic by the Medical Surgical and Orthopedic Services. Amphitheater Children's Hospital

\*Open to the medical profession

MARCH 15-SEPTEMBER 15 Boston University Course for Discharged Medical Officers Page 240 issue of February 14

APRIL 1-JUNE 1 Intensive Course in Ophthalmology Page 240, issue of February 14

MAY 29 New England Obstetrical and Gynecological Society Page 616 issue of May 2

JUNE 3 New England Heart Association Notice above

JUNE 6 New England Hospital for Women and Children Notice above

JUNE 20-22 American Association for the Study of Goiter Page 312, issue of February 28

JUNE 29 American College of Chest Physicians Page 544 issue of April 18

JULY 3 Harvard Medical Alumni Association Page 682 issue of May 16

SEPTEMBER 4-7 American Congress of Physical Medicine. Page 616, issue of May 2

OCTOBER 7-18 New York Academy of Medicine. Page 544 issue of April 18

# The New England Journal of Medicine

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## ETHER INHALERS IN EARLY USE

WILLIAM W FORD, M.D.\*

BALTIMORE, MARYLAND

ON A brick building at 17-19 Tremont Street, Boston, an inconspicuous bronze tablet commemorates the first of two events that served to introduce ether anesthesia and thereby changed the history of surgery. The tablet is inscribed as follows "On Sept 30, 1846, in a room in this building, Dr William Thomas Green Morton first demonstrated the value of ether as an anaesthetic in a dental operation." A little more than two weeks from this date, on October 16, 1846, Morton, a successful dentist of twenty-seven who was also an enrolled student of medicine at Harvard, gave his epochal demonstration of ether as a pain-relieving agent in an operation for a vascular tumor of the neck, performed by Dr John Collins Warren.

Following this discovery ether inhalers were produced in great variety and number. They included intricate and costly pieces of machinery, as well as mere bladders equipped with an inhaling tube and mouthpiece. The earliest of these inhalers, after Morton's, were brought out in this country, although Morton's instrument remained the only one in general use here. Many of the earliest, if not the most elaborate, ether inhalers in Europe were those produced in England, where the foundations of our modern scientific knowledge of anesthesia were laid through the work of John Snow.

In the dental operation of September 30, 1846, Morton administered ether by means of a saturated handkerchief given to the patient, Eben H Frost, to inhale when he asked to be mesmerized before the extraction of an ulcerated tooth. During the interval, however, between this highly successful experiment and the operation at the hospital, Morton having applied to Dr Warren on October 5 for permission to demonstrate his compound, a search was made for a suitable inhaling apparatus. Morton apparently had previously been interested in methods of inhaling, this interest, according to his own statements, dating back to the summer of 1844. At that time, when he was a medical student under Dr Charles T Jackson prior to his admission to Harvard, and as a result of Jackson's suggesting

ether when he was filling a tooth for a patient, he pored over the ether literature he found in Jackson's library and began his self-experiments with the drug, hoping to prove it an alleviator of pain in dentistry.

Aside from Pereira's *Materia Medica*, there are no specific references concerning Morton's reading at this period, but he might easily have come across such references to ether inhalation as those of Richard Pearson, Thornton and Nyvsten among others. During the 1830's and early 1840's, moreover, there was a good deal published, including the writings of Scudamore and Corrigan, on the inhalation treatment of diseases of the respiratory tract. Frequently there was some mention, if not a description, of apparatus for the inhalation of iodine, chlorine and other vapors. Above all, any early ideas he may have entertained on the subject of anesthesia in dentistry were greatly strengthened in January, 1845, by his witnessing the demonstration (technically a failure) of nitrous oxide gas by Horace Wells, his former dental instructor and partner.

Late in the summer of 1846, after various experiments, which Morton claimed included some on his dental assistants as well as on animals, had failed to produce any conclusive results and he was "much discouraged," he determined to procure a satisfactory form of apparatus. To this end he had several conferences with Joseph Wightman, maker of philosophical instruments on Cornhill. Morton<sup>1</sup> stated

While examining his bags for inhaling nitrous oxide gas, the thought struck me that I could put the ether into one of these, and by making an opening to be closed by a valve, for the admission of atmospheric air, could convert it into an inhaling apparatus. Upon second thought I had an impression that ether would dissolve India rubber, and put the question to Mr Wightman. He thought it would. I then put the same question as to oil silk.

Wightman, it is said, advised him to get the opinion of a chemist, suggesting that he consult his former preceptor, Dr Jackson, who was a chemist and geologist of note as well as a physician. This Morton did, and the interview, which was based on certain inquiries concerning ether, provided Jackson with what he regarded as a conclusive argument in favor

\*The late William W Ford, M.D., D.P.H., was emeritus professor of epidemiology, School of Hygiene and Public Health, Johns Hopkins University.

of his own later claim to priority of discovery. At about that time Morton also conferred with N B Chamberlain, an instrument maker of School Street, in regard to inhalers.

Dr Jackson, perhaps recalling Faraday's<sup>2</sup> statement, "A convenient mode of ascertaining the effects is obtained by introducing a tube into the upper part of a bottle containing ether, and breathing through it," had first suggested a simple flask with a glass tube inserted in it. Morton reported that he attempted to employ this device in a self-experiment shortly before his operation on Frost but completed the experiment by inhaling the ether from his handkerchief. Jackson later advised the use of a flask

the apparatus, was not yet satisfied. His anxiety, in fact, became so great that on the evening before his demonstration at the hospital he consulted Dr Augustus A Gould, a member of the Massachusetts Medical Society and one of his most sympathetic and helpful advisers. Dr Gould suggested the employment of valves to control the flow of air, and together with Morton and Wightman spent the better part of the night making sketches of new apparatus. At daybreak of October 16, Morton took the final design to N B Chamberlain and persuaded him to set to work on it. A little before ten o'clock — the hour of his appointment at the hospital — he left Chamberlain's shop carrying a new

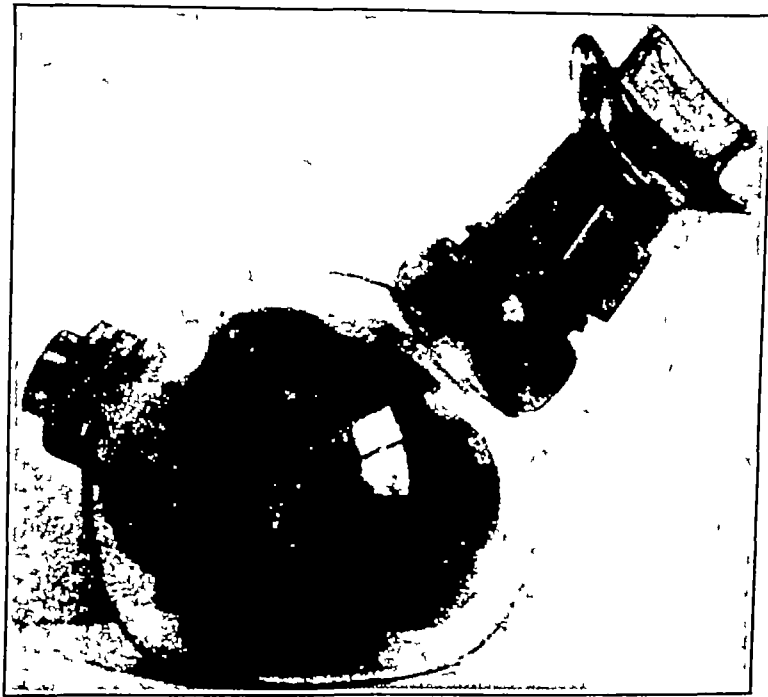


FIGURE 1 Morton Ether Inhaler (1846)

*This model is the one generally considered to have been used by Dr Morton at his first public demonstration of ether anesthesia at the Massachusetts General Hospital on October 16, 1846 (Courtesy of the Massachusetts General Hospital)*

with a bent glass tube 3 feet long, but this proved unsatisfactory and Morton obtained from Wightman a tubulated globe receiver employed in distillation. A piece of sponge moistened with ether was put in the larger end of the globe, and a wooden tube for a mouthpiece was added, the patient's nostrils being compressed between the thumb and finger of the operator or dental assistant.

After this apparatus had been employed for several tooth extractions, with varying degrees of success, Wightman introduced a cork in the tubulure, through which a dropping tube was inserted, notches having been cut in the cork for admission of air and for pouring the ether. But Morton, always speculating on the possibility of asphyxia from

inhaler, the description of which he<sup>3</sup> later published with the following detail:

The apparatus [Fig 1] consisted of a glass vessel, about six inches square, with rounded corners, one opening, two inches in diameter, was left on the top through which a sponge was inserted and the ether poured, and another, an inch and a half in diameter, on one side for the admission of external air. On the side opposite the last-named opening was a glass tube, two inches in diameter, and an inch in length, terminating in a metal mouth piece three inches long, and of the same calibre as the glass tube. This mouth-piece was provided with two valves, one covering a circular opening, three quarters of an inch in diameter, on the top, and the other extending across it. These valves were so arranged that, when the patient filled his lungs, the upper valve shut down, closing the aperture in the top of the mouth-piece, while the one across the mouth-piece opened and allowed the ethereal vapor, mixed with atmospheric air, to pass into the lungs, and when he emptied his

lungs the pressure of the expired air closed the valve across the tube, while the same pressure opened the upper valve, and allowed the vapor, which had once been breathed, to pass into the room, instead of returning into the reservoir

Miller<sup>4</sup> has stated that the principle of Morton's inhaler has been but slightly improved in all the succeeding years. With some modifications the instrument was employed by Morton for the first six months after the discovery of anesthesia, he then turned to the use of the sponge

Accompanied by Eben H. Frost, as a former patient who had successfully inhaled ether on September 30, 1846, Morton, out of breath and a quarter of an hour late, on the historic morning of October 16 reached the surgical amphitheater in the Bulfinch Building of the Massachusetts General Hospital, where the assembled surgeons, medical students and the patient, Gilbert Abbott, a frail youth of twenty in a plush upholstered reclining chair, awaited his coming. After Morton had given Dr. Warren — who was on the point of operating without further delay — the reason for his tardiness, he filled the new inhaler with ether mixed with "French essence" to disguise its odor and anesthetized Abbott, with the success attested to by Dr. Warren's never-to-be-forgotten remark, "Gentlemen, this is no humbug."

Following the demonstration Morton was invited by the surgeons to administer ether for an operation on October 17, but before doing so he acted on a suggestion of Dr. Gould's concerning a still better valvular system for his inhaler, with the result that the second operation (the removal of a fatty tumor from a woman's arm) was even more successful than that of the preceding day. After these trials the use of the anesthetic was discontinued at the hospital until November 7.\* In the meantime, Morton devoted himself to giving ether in his dental practice and soon had a record of one hundred and sixty dental operations to his credit. Within a few weeks he found it necessary to enlarge his office and take all the space available at 19 Tremont Row.

On November 7, 1846, came the supreme test of Morton's remedy — an amputation of the thigh. "Everybody awaited this test by amputation, and then only was the accumulated evidence deemed conclusive," wrote Henry J. Bigelow.<sup>6</sup> Dr. Bigelow, who was present at the operation of October 16 and witnessed several dental operations in Morton's office, announced the great discovery in a paper read before the Boston Society for Medical Improvement on November 9. But previous to that date, on November 3, he had read an abstract of the paper at a meeting of the American Academy of Arts and Sciences, and the paper in its entirety was pub-

lished in the *Boston Medical and Surgical Journal* of November 18, 1846.<sup>7</sup> Less than a month before, this journal<sup>8</sup> had printed the brief notice later to be so frequently quoted: "Strange stories are related in the papers of a wonderful preparation, in this city, by administering which, a patient is affected just long enough, and just powerfully enough, to undergo a surgical operation without pain." This was the first notice of anesthesia to appear in any medical publication.

Morton, endeavoring to keep his compound a secret one, had been informed, prior to the amputation of November 7, that the surgeons must be told the nature of the substance used before its further employment at the hospital, and in a letter to Dr. Warren — whom he had already informed — he had made the announcement that he was employing sulfuric ether. The mention of sulfuric ether also occurred in the patent for the discovery, applied for jointly by Morton and Dr. Jackson on October 27, 1846, and granted on November 12 of that year. Morton, however, still lacked a specific name for his compound, and a meeting was held at Dr. Gould's house on November 20 for the purpose of selecting one. "Letheon" (derived from a Greek word *lêthê* meaning oblivion, the name of one of the rivers of hell, of which the souls of the dead were supposed to drink, inducing forgetfulness of the past, after they had been for a certain time confined in Tartarus, a region of Hades) was on a list of names submitted and was immediately chosen by Morton. The term "anaesthesia," likewise of Greek origin, did not seem to interest him when it was proposed on the following day by Dr. Oliver Wendell Holmes, who had been present at the meeting.

Letheon served both as a name for ether and as a designation for the unique series of advertisements, circulars and pamphlets relating to the discovery, that Morton published from the latter part of November, 1846, to May, 1847, some of the earliest of these notices appearing in the advertising pages of the *Boston Medical and Surgical Journal* and the *Boston Evening Transcript*. The first description of the Letheon publications, some of which have become excessively rare, was given by Benjamin Perley Poore<sup>9</sup> in *Historical Materials for the Biography of W. T. G. Morton*, published in 1856. In 1858 practically the same account appeared in Nathan P. Rice's *Trials of a Public Benefactor*.<sup>10†</sup>

Terms derived from Letheon also served to designate the ether inhaler and the method of administering the drug, namely "letheonic apparatus" and "letheonising." These terms were used, perhaps for the first time, in the communications of James A. Dorr, an American residing in London and one of the special agents employed by Morton while he was attempting to enforce his patent here and

\*According to Hodges,<sup>5</sup> Morton never gave ether for more than five or six operations at the Massachusetts General Hospital, although he consented to administer it to some extent for operations performed by the hospital surgeons and others in private practice. Dr. Henry J. Bigelow, having conducted extensive experiments and become thoroughly familiar with the use of ether anesthetized the majority of patients undergoing operations at the hospital during the year following the introduction of anesthesia.

†A bibliographical description of these publications listing them for the first time in the order of their appearance, has been given by Dr. John F. Fulton under the title, *The Morton and Warren Tracts on Ether (Letheon)*, which was published as an appendix in *The History of Surgical Anesthesia* by Thomas E. Keys (New York: Schuman's, 1945).

abroad and to control the use of ether by the sale of licenses and inhalers for its administration in surgery. By virtue of his identification with the Letheon pamphlets, the most prominent of these agents was Edward Warren,\* who represented Morton's interests in Washington and Paris and edited three editions, running into five issues, of the pamphlets under the title, *Some Account of the Letheon*.

Despite strong medical opposition to anesthesia, exemplified in a much-quoted editorial, with its charges of quackery, in the *Philadelphia Medical Examiner* for December, 1846, as well as similar pronouncements in such publications as the *Annalist*,<sup>12-14</sup> a New York journal, and the *New Orleans Medical and Surgical Journal*,<sup>15</sup> — to say nothing of attacks by the dentists, headed by Dr J F Flagg, of Boston, — Morton's inhaler was widely distributed. Through his own efforts or those of his agents, it appears to have come into fairly extensive use in this country within four or five months after his initial demonstration of ether. The use of the instrument, together with ether, was offered free to all charitable institutions.

The drug was employed at an early date for several operations, including an arm amputation, by Dr Abel L Peirson, the leading surgeon of Salem and Essex County, whose report of his cases<sup>16</sup> — all successful — was the first account of private surgical operations under anesthesia to be published. Dr Peirson's use of Morton's inhaler is implied by the statement that the anesthetic was administered by a dentist, Dr Fisk.

Among the first surgeons of prominence outside of New England to make use of the instrument was Valentine Mott, of New York City, who tested it with success in operations for tumor and anal fistula in December, 1846, the earliest of these being performed on December 8. Other operations were performed in New York City by Dr A L Cox,<sup>17</sup> an early and enthusiastic advocate of Letheon. All the first experiments there were supervised by Dr Horace Kimball, a dentist, who acted as Morton's agent and used the apparatus in his own practice. About the middle of January, 1847, ether analgesia by means of the inhaler was tried at the New York Hospital. But the existence of the patent and the concealed nature of the remedy — for even when it was known to be sulfuric ether a certain aura of mystery surrounded its preparation for a time — rendered Letheon unpopular in New York and hampered the immediate adoption of anesthesia in that city.

With the spread of anesthesia in the South and West during the winter of 1847, Morton's inhaler was introduced in such cities as New Orleans, St Louis and Cincinnati, the instrument, strangely enough, figuring in a fatal case of chloroform in-

halation† occurring in Cincinnati a year later. The early tests of ether in these cities were apparently highly successful, and in New Orleans the editors of the *New Orleans Medical and Surgical Journal*, who had witnessed the first operation under ether there — a thigh amputation performed at the Charity Hospital on February 25, 1847 — promptly reversed their unfavorable judgments concerning the discovery.

In Georgia, where Dr Crawford W Long performed the first surgical operation under ether anesthesia in March, 1842, using a saturated towel and from time to time performed other operations under the drug but did not publish his findings until 1849,<sup>21</sup> successful experiments, with a handkerchief the favored means of administering ether were conducted at the University of Georgia and the Georgia Medical College following the announcement of Morton's discovery. Paul Fitzsumner Eve, professor of surgery at the Georgia Medical College, co-editor with Dr I P Garvin of the *Southern Medical and Surgical Journal* and one of the vice-presidents of the National Medical Association, appears to have been the first of the Georgia physicians to investigate the discovery at this time, making inquiries concerning it as early as November, 1846.<sup>22</sup>

Some tests of ether took place in Baltimore in the late autumn of 1846, although the first Maryland physician to adopt the use of anesthesia was a young surgeon in Frederick, Samuel M Tyler.<sup>23</sup> The early Baltimore experiments were not so successful, perhaps owing to impurities in the ether. A handkerchief or sponge in preference to the inhaler was employed there, as in Philadelphia, where the first surgical operation under the drug — a finger amputation performed by Dr William Gibson — did not occur before May, 1847. According to Parrish,<sup>24</sup> however, a number of reputable Philadelphia dentists had employed ether regularly in their practice for several months previous to that date.

As stated earlier, a number of inhalers made their appearance in this country shortly after Morton's late in December, 1846, — a time when ether was often referred to as the "new gas," — the *Boston Medical and Surgical Journal* published<sup>25</sup> the following

In the face of the patent instruments used in administering the gas, made principally of glass, with metallic fixtures, such as a mouth piece, valves, etc., are manufactured in this city to a great extent. One person assured us that the demand far exceeded his ability to manufacture the article. Several individuals not only advertise that they prepare the *air of forgetfulness*, but that they have the apparatus also — and from what is bruited about the town, a thriving business is conducted by those who stand in no fear of patents. Some of the artists consider that the administration, only, was secured by the

\*Warren's own dislike for the term "agent" as applied to his association with Morton was expressed in a contemporary issue of the *Boston Medical and Surgical Journal*.<sup>11</sup>

†That of Mrs Martha G Simmons, thirty-five years of age, and apparently in good health, who died within ten minutes after inhaling chloroform for a dental operation. The anesthetic was inhaled from a saturated sponge placed in Morton's apparatus and filling about a third of the glass globe. This fatality, which occurred on February 23, 1848, and was reported in full in the *Western Lancet*<sup>18</sup> and the *St Louis Medical and Surgical Journal*,<sup>19</sup> attracted wide attention.

patent, and not the instrument, others are of the opinion that such a gas-holder as they produce, is no infringement of a right secured to others, inasmuch as their work is an invention of their own

It appears that not a few inhalers reached the Massachusetts General Hospital "After its acceptance of the discovery," wrote Hodges,<sup>26</sup> "the hospital was overwhelmed with inhaling apparatuses of

ber 13 of that year, however, he and Dr Augustus A Gould took out a patent for an apparatus\* "to be used for the purpose of administering to persons or introducing into their lungs the vapors of ether or various other chemical matters" Features of this inhaler included an evaporating vessel with a special system of induction and eduction valves, a

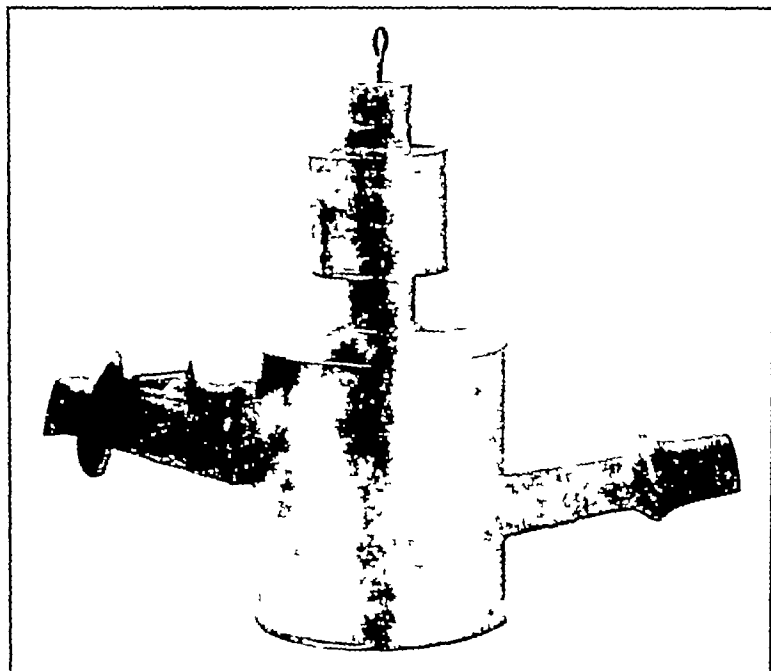


FIGURE 2 Morton and Gould Ether Inhaler (Photograph from United States National Museum)

This was protected by U S patent 5365, issued on November 13, 1847 The model is entirely made of tinned metal, with the exception of the cork used as a stopper in the metal reservoir (which could also be made of glass or other suitable material) and the sponge The mouthpiece, with a supporting flange or lip, is shown on the left, attached to the evaporating vessel, which contained the sponge

every device and size — most of them cumbersome and expensive — sent them by the makers It is to be regretted that these contrivances were not preserved, as they would now be interesting curiosities"

Morton himself, at first sufficiently persuaded that the inhaler was the best means of administering ether, if not indispensable to the success of his discovery, contracted for hundreds of sets of apparatus, as well as globes, retorts and other glassware for each modification of his instrument All these were to be left valueless on his hands with the adoption of the conical sea sponge, employed at the Massachusetts General Hospital by J Mason Warren<sup>27</sup> in March, 1847, and introduced in England at about the same time Morton bowed to the inevitable and substituted the sponge for his inhaler, warmly praising this new medium in a letter to the *Lancet*, published July 17, 1847 On Novem-

ber 13 of that year, however, he and Dr Augustus A Gould took out a patent for an apparatus\* "to be used for the purpose of administering to persons or introducing into their lungs the vapors of ether or various other chemical matters" Features of this inhaler included an evaporating vessel with a special system of induction and eduction valves, a

\* \* \*

Meanwhile the instrument makers in Europe had not been idle The news of the discovery had reached London in the middle of December, 1846 On November 28, Dr Jacob Bigelow, the father of Dr Henry J Bigelow, sent a letter giving an enthusiastic account of the ether demonstration and subsequent operations at the Massachusetts General Hospital to Dr Francis Boott, of London, a physician with many Boston affiliations and Bigelow's personal friend He likewise dispatched a copy of the *Boston Daily Advertiser*, which contained an

\*A model of this apparatus in tinned metal is now in the Smithsonian Institution, United States National Museum A complete account of it has been given by Dr George B Roth<sup>28</sup> It is here reproduced (Fig. 2) through the courtesy of Mr J E Graf assistant secretary and Dr Charles Whitebread associate curator of medicine, Smithsonian Institution

article by Dr Henry J Bigelow announcing the discovery, first published in the *Boston Medical and Surgical Journal* of November 18. Receiving these communications on December 17, Dr Boott lost no time in informing his associates, including the Gower Street dentist, James Robinson. Private letters from Dr John C Warren and Dr John Ware sent to the *British and Foreign Medical Review* reporting the discovery were also received about that time, and the inhalation of ether became the "all-engrossing subject."

On December 19, Robinson gave ether to Miss Lonsdale, a relative of Dr Boott's, and painlessly extracted a molar tooth. The inhaler used on this occasion consisted of the lower part of Nooth's apparatus (used for making soda water) with a flexible tube, to which was attached a ball-and-socket valve and a mouthpiece resembling those generally employed for inhalation. It was later referred to by Robinson<sup>29</sup> as "a very imperfect apparatus, hastily got up, and which was condemned from its ill success in cases on the 20th." Another form of the inhaler was promptly devised by Dr Boott and Robinson and made by William Hooper, a chemist and instrument maker in Pall Mall.

Employed in many of the earliest experiments carried out in London and undergoing various modifications, the inhaler in its general form consisted of two stoppered glass vessels, taken from the popular Nooth's apparatus. The vessels contained pieces of ether-saturated sponge, cut into triangular shapes and arranged in such a manner as to present as large a surface as possible for the rapid evaporation of the ether. The vapor was conveyed through an elastic inhaling tube, with a pad to be held over the mouth to prevent the breathing of free "atmospheric air," a point stressed by the designers. The pad was kept in place by the operator or his assistant. A stopcock attached to the mouthpiece regulated the volume of the ether vapor, and a nose spring, which practically all European inhalers featured in one form or another, compressed the nostrils when necessary.

This instrument was well publicized during the first months of ether inhalation in Europe, reproductions or references to it appearing in the *Illustrated London News* of January 9, 1847, the *Lancet* of January 16, the *London Medical Gazette* of January 29, the *Gazette des Hôpitaux* of February 13 and other journals. A cut of the inhaler in its improved form was also reproduced in Robinson's *Treatise*, published in the spring of 1847.

On the day of the first tooth extraction — Saturday, December 19 — Robert Liston, informed of the discovery by Dr Boott, called on his friend Peter Squire, a well known London chemist, with the unusual request to have an inhaling apparatus made ready for a surgical operation — an amputation of the thigh — to be performed under ether narcosis on the following Monday. It was then past mid-

day, but Squire met the emergency. Like Robinson, he employed a Nooth's apparatus. The upper detachable cylinder was packed with pieces of sponge, and a flexible tube with an ordinary bronchial inhaler mouthpiece was fastened to the exit, the patient's nostrils being held by the fingers. Saturating the sponges with ether, Squire, after some preliminary difficulty, completely anesthetized his nephew, William Squire, later Dr William Squire, F R C P, who had volunteered his services as a subject for inhalation.

On December 21, 1846, the first successful surgical operation under anesthesia in Europe, so graphically described by F William Cock,<sup>30</sup> took place at the University College Hospital in London. Liston, then at the height of his distinguished career but to die before another year was out from an aortic aneurysm, amputated the limb with his accustomed skill and rapidity after the patient had been placed under the influence of ether by William Squire, using the elder Squire's inhaler. Among the students thronging the amphitheater on this occasion and hearing Liston — wildly enthusiastic — predict that in six months no operation would be performed without ether was Joseph Lister.

Within the next few days James A. Dorr informed the medical profession and the public of Morton's patent rights by means of a letter addressed to the *Lancet* stating, "that the process for procuring insensibility to pain by the administration of the vapour of ether is patented for England and the Colonies, and that no person can use that process, or any similar one, without infringing upon the rights legally secured to others." This statement was published with other early notices of anesthesia that appeared in the *Lancet*.<sup>31</sup>

The patent at once became the cause of a great deal of unfavorable comment and misunderstanding in Europe, as it had in this country, and efforts to have it recognized met with little success, as may be judged from the following notice of Dorr's,<sup>32</sup> issued on January 30, 1847, and printed in the *Pharmaceutical Journal and Transactions* under the heading "Letheonic Apparatus."

I feel it to be a duty to inform the Medical and Surgical Profession, and the Public in general, that in order to insure the safe use of the Letheon, certain conditions rigorously are necessary in the apparatus employed. It is possible to strangle instead of letheonising, and I would therefore urgently advise every operator, whether licensee or infringer, to be careful that all the air-passages of the apparatus used be of large diameter. This diameter should not be in any part less than three-eighths of an inch bore, and particular attention should be given that there is no obstruction to the free circulation of air or vapour through the valves. I regard the practice of compressing the nostrils of a patient, by means of a spring or other instrument, as highly dangerous and improper. The nostrils should be closed by the fingers of a prudent and experienced person. *Asphyxia and etherisation are two very different things.* It is trusted that no one will be so ungenerous or so unwise as to construe this information, which is communicated from motives of humanity, into an abandonment of any lawful claim.



his was signed by Dorr as agent for the proprietors of the *Letheon*

Other notices and letters of Dorr's in defense of his patent and Morton's claims to priority of discovery, several of which were published in the *Lancet*, continued to be issued during the winter of 1847. He also prepared, according to Rice,<sup>23</sup> a number of sets of expensive apparatus with full instructions for their proper use. These, in accordance with the custom prevailing in monarchical countries, he forwarded in Morton's name to the principal European rulers, as well as to many surgeons of prominence.

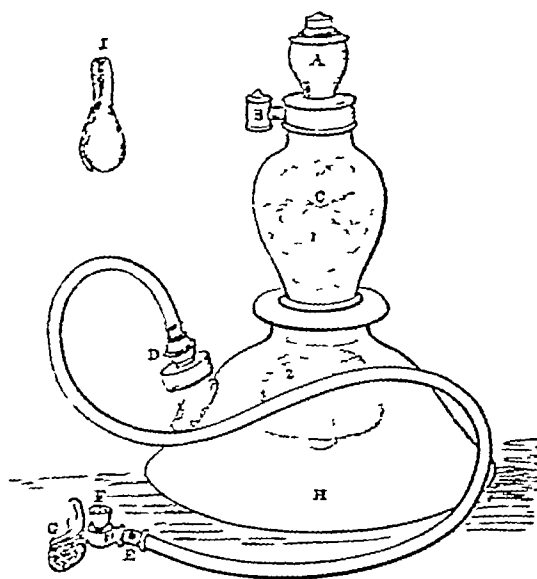
Following Liston's trial of anesthesia, Peter Squire reconstructed his inhaler, employing special patented valves (Read's valves), so arranged as to prevent the expired air from returning into the apparatus, a ferrule near the mouthpiece for regulating the quantity of air admitted and a spring for closing the nostrils. The inhaler, a glass urn, was supplied with ether at the top by means of a metal funnel that formed part of the stopper of the urn. The ether fell through a nozzle and was distributed in a shower on the sponge. Too rapid evaporation of the anesthetic was prevented by the patented valve in this part, which admitted air at each inspiration and then closed instantly. The mouthpiece, made at first of wood and later of glass or metal, was constructed to fit the mouth and entirely enclose it.

With all its carefully executed detail, this apparatus was one of the more elaborate, if not the most costly, of the many inhalers exhibited and discussed at a meeting of the Pharmaceutical Society held in London on January 13, 1847, — when interest concerning the successful administration of ether by an instrument was at its height. The meeting was well attended, the lecture room of the society being crowded with members and medical men who had gathered to hear Squire read a paper<sup>24</sup> that presented a general discussion of the subject of inhalation and gave an account of his own instrument (Fig 3), which became one of the principal English inhalers of the period.

Dividing the honors with Squire's apparatus was the inhaler of Boott and Robinson, also exhibited on this occasion and discussed by Hooper, who had introduced several modifications and offered it as an instrument employed in a large number of cases without failure. An elaborate system of valves and an improved nasal spring had been added to Nooth's glass apparatus. A special feature was the reconstructed pad for the mouth, this pad, later described by Robinson<sup>25</sup> in his treatise, was so flexible that by pressing its edges the operator could fit it to a mouth of any size without difficulty. It was made of thin sheet copper, covered with soft leather on the inside, which was thickly stuffed and padded with wool. An opening in the center of the pad provided for an ivory or amber mouthpiece to be screwed on and kept in the mouth during inhalation.

An instrument with similar features continued for some time to be manufactured by Hooper and bore his name.

Other forms of apparatus shown at the meeting, a number of which were subsequently reproduced in the *Pharmaceutical Journal*, included a wide variety of urns, jars, cylinders and funnels, with fittings of amber, ivory, brass, ebony, pressed steel, tin and vulcanized rubber. Bladders were also in favor and



- A The Urn with its stopper into which the ether is poured.
- B Valve which admits the air
- C Contains sponge saturated with ether
- D Valve which opens at each inspiration, and closes at each expiration
- E Ferrule for regulating the quantity of atmospheric air admitted.
- F Valve for the escape of expired air
- G Mouth-piece.
- H Lower case.
- I Spring for closing the nose.

FIGURE 3 Squire's Ether Inhaler (1847)

were recommended for the use of dentists on account of their simplicity. They possessed the additional advantage of not being protected by patents or caveats. Ivory mouthpieces were popular, and silver was also used in some instances. A mouthpiece of glass was advocated by Jacob Bell, editor of the *Pharmaceutical Journal*, who<sup>26</sup> expressed the opinion that some persons might object to apply to their mouths a pad or wooden tube saturated with moisture from the patient who had used it last. The glass mouthpiece could be removed and as easily washed as a cup or wineglass.

Interested in obtaining a simple apparatus that would serve its purpose economically, since many instruments had been designed without thought of the expense, Bell had constructed an inhaler from an ordinary green quart bottle. This had a bung with two openings, through one of which a glass tube for conveying the ether vapor passed nearly to the bottom of the bottle, the other opening being

fitted with an inhaling tube and valves. The glass mouthpiece, similar in form to an eyeglass or cup, although somewhat larger, was to be added to the inhaling tube. In place of a sponge a little water was introduced into the bottle with the ether, through which the bubbles of air passed from the lower end of the glass tube, thus becoming saturated with the vapor. This apparatus, as exhibited at the meeting, was recommended as one easily put together by a surgeon in the country who could not command the facilities of a London hospital. A modified and more elaborate form of this apparatus (Fig. 4) was later brought out by Gilbertson, a London designer who had assisted Bell in the production of the first instrument. In the illustration two types of glass mouthpiece are seen.

Bell believed that skill and practice were prerequisites to the really successful inhalation of ether, so that failure in some cases should not always be

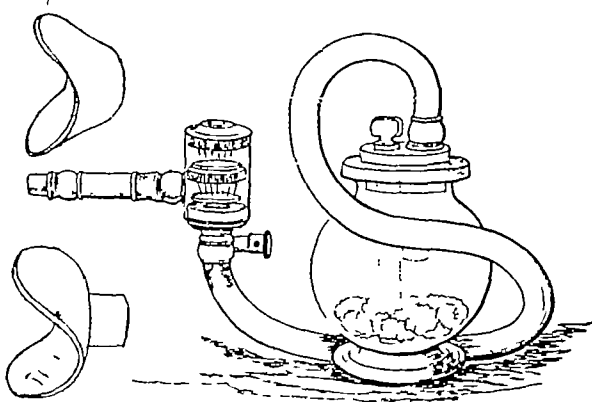


FIGURE 4 Gilbertson's Ether Inhaler (1847)  
*Two types of glass mouthpiece are to be seen on the left*

attributed to the instrument employed, an opinion that Squire had also expressed and one that was shared by others at that time.

Still another form of simple apparatus with an element of novelty was an adaptation of the German pipe, offered by Tracy, of St. Bartholomew's Hospital, who during the course of some seventy or eighty tooth extractions had first tried many of the usual types of inhalers. The general efficacy of these instruments when properly employed he considered as being on a high level, for when failures had occurred he believed, with Squire and Bell, that the patient was perhaps at fault. But he regarded the size of most of the inhalers as an objection, especially in the extraction of teeth, a procedure in which the operator should be able to administer the vapor without the aid of assistants and easily dispose of the instrument when the patient was once under the influence. Therefore, with the hookah first in mind, Tracy had adopted the German pipe as meeting

the desired requirements. This pipe (Fig. 5) was made of glass, mounted at the top with a brass cap and stopcock, into which was screwed a sixteen-inch elastic tube. The tube was surmounted by a double-valve mouthpiece, and a padded steel compress

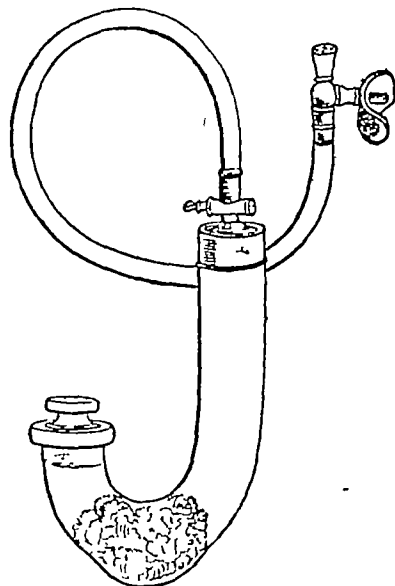


FIGURE 5 Tracy's Ether Inhaler (1847)  
*This is constructed on the lines of a German pipe*

served for securing the nostrils. As much ether was poured into the pipe as would fill the well and saturate the sponges. The mouthpiece was placed between the patient's teeth, the stopper removed, the stopcock turned on, and the patient directed to inhale in the natural way. In subsequent accounts of the instrument, Tracy<sup>37</sup> stated that he had used it for a large number of operations and had found it better than any other apparatus he had employed.

The inhaler had been constructed by Ferguson, the instrument maker to St. Bartholomew's Hospital, who had supplied all previously used by Tracy and was among the designers having three or more varieties of inhalers on display at the meeting. Reporting on this meeting, the *Lancet*<sup>38</sup> published the following comment in regard to the number of instruments shown, "they were really so numerous, that it would appear that the whole scientific portion of the members of the Society, as well as that of many others, had been employed in inventing and contriving means for administering the vapour of ether." Nevertheless, still more inhalers were to be introduced, including John Snow's water-heated apparatus, of which there will be further mention.

Such instruments as Startin's "Pneumatic Inhaler," with a brass nose spring and a special fumigating device, which could be substituted for the

ether chamber or reservoir of the inhaler, some other substance than ether being employed, came into popular use for a time, as did two inexpensive tin inhalers, one of them portable (Fig 6), devised by Alfred Smee, F R S. The portable inhaler — one of the earliest — was severely simple, consisting of

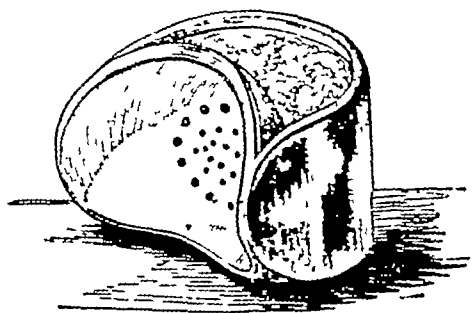


FIGURE 6 Smee's Portable Ether Inhaler (1847)

little more than a metal mouthpiece to which was attached a small pouchlike receptacle of the same material for holding the ether and sponge. In the first form of this instrument, however, no provision

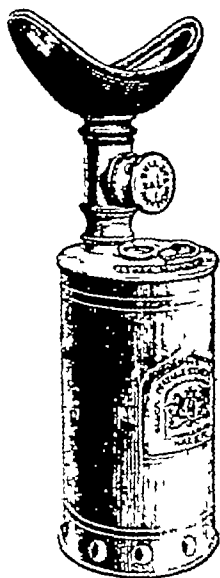


FIGURE 7 Salt's Portable Ether Inhaler (1847)

The top was pulled out and the ether was poured on the sponges in the metal cylinder, the top then being replaced. With the air holes, ether partially or entirely exposed, the inhaler was then ready for use.

had been made to prevent the possibility of the ether from running into the mouth during inhalation. Hedley's wooden inhaler, although not classified as portable, was another compact instrument. It was a cylinder about nine inches in length, shaped

at one end to form a mouthpiece and made of box-wood, lignum vitae or cherry, with valves of the same material. The latter were placed near the mouthpiece, the ether being received from a sponge introduced into the body of the instrument. More elaborate, but advocated as of convenient size and form for the pocket, was Salt's portable inhaler (Fig 7), produced at Birmingham. By means of a revolving plate with corresponding openings, fitted into one end of the cylinder or body of the apparatus, and through the alternate admission of air and ether, the volume of the vapor could be regulated without removing the instrument from the mouth. The other end of the cylinder was fitted with a revolving tube, which also had corresponding apertures for controlling the quantity of air admitted. To prevent evaporation, both ends of the apparatus could be closed when it was not in use.

Gallard's portable instrument (Fig 8) was a cylindrical tin box, the lid of which contained an

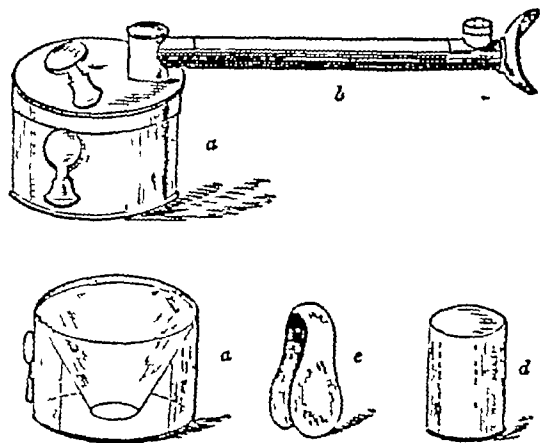


FIGURE 8 Gallard's Portable Ether Inhaler (1847)

a is the cylindrical tin box, b, a tube of sufficient caliber to permit a two-ounce bottle of ether to be packed in it, thus forming a case, c, the mouthpiece and valves, d, one of the caps to tin tube used as a bottle case, and e, the brass clip for closing the nostrils.

adjustable hole for the admission of air in almost direct communication with the tube. The box itself also had an adjustable hole for admitting air in closer connection with the ether. The tin inner lining of the box, which was conical in shape, allowed two or three ounces of ether to remain in it without spilling, whereas a small inside tube provided for the ether to be poured back if not wanted. A mouthpiece, valves and a brass nose clip, not unlike a pair of sugar tongs, completed the apparatus. All parts of it, with the exception of the tube, were made to fit into the box. When opened, the larger hole supplied the ether vapor in diluted form, and the smaller one a much more concentrated vapor. The holes could be closed during each expiration.

but were supposed to be opened by the anesthetist before each inspiration

A variety of portable inhalers — some as small as four and a half by two inches — were soon being made. They were regarded as especially appropriate for women and, fitted into morocco or other suitable cases, proved popular at gatherings where ether was inhaled for exhilarating purposes only. Portable models that had the basic features of their principal inhalers were brought out by Squire, Hooper and later by John Snow. Hooper likewise designed what was perhaps the first inhaler for horses. This instrument was formed of a specially constructed muzzle with inhaling tube and valves, with a vulcanized rubber bag attached for holding the ether and sponge. The whole was adjusted to the animal by means of a headpiece, similar to a bridle, and a tightly fitting rubber band placed over it near the top.

Squire's large inhaler was apparently the first to come into use in Edinburgh. The instrument had been dispatched by Liston to his friend James Miller, who performed the initial operation under anesthesia in Edinburgh at the Royal Infirmary.<sup>39</sup> This took place about the middle of January, 1847. The discovery excited great interest among the Scots and various forms of inhaling apparatus were soon being tested — although not always successfully — in surgical procedures. In Edinburgh, as in Dublin,\* a simple form — the glass jar or flask variety, with or without valves, seemed to be the preferred type of inhaler and was chosen by such men as James Y. Simpson and James Syme.

Simpson, who introduced the use of ether in obstetrics on January 19, 1847,<sup>41</sup> employed a portable glass flask without valves, which contained ether, poured on a piece of flannel or other absorbent material. The flask had a mouthpiece and an aperture in the side to admit air. He continued to make use of this device or a concave sponge in administering ether until his introduction of chloroform anesthesia in November, 1847,<sup>42</sup> when he gave the anesthetic on a handkerchief. (In his original patent of 1846, Morton, it may be said, had listed both the sponge and the common glass flask as among the effective methods of giving ether.)

Syme, prompt in his employment of anesthesia as he was in his later adoption of asepsis, following the precepts of his son-in-law and greatest pupil, Joseph Lister, used practically the same ether apparatus as did Simpson. But he had previously experimented with other apparatus, which gave such poor results that he<sup>43</sup> states, "in common with many members of the profession, who had experienced similar discouragement, I resolved to abandon the use of ether, at all events until better results could be obtained." After the advent of John Snow in the field of anesthesia and his success, Syme was suf-

ficiently encouraged to recommence his own employment of ether, which he did successfully, although, one of the first besides Pirogoff to adopt anesthesia in Europe, he maintained a somewhat conservative attitude in regard to its uses for a time.

James Kemp, a philosophical instrument maker of Edinburgh, constructed a portable inhaler that was included among five principal inhalers listed by the *Edinburgh Medical and Surgical Journal*<sup>44</sup> in the following order: Squire's ("the one most commonly employed in the Metropolitan hospitals and in London generally"), Snow's, Startin's, Robinson and Boott's, and Kemp's.

Kemp's inhaler, fitted into a case ten inches by four, was similar to the German pipe of Tracy's apparatus and consisted of three parts — a strong bent syphonlike tube for holding the ether, a stopcock for preventing evaporation when the instrument was not in use, a flexible tube with the usual inspiratory and expiratory valves and a mouthpiece. The tube could be made of glass, block tin, brass or any other suitable material, and was large enough at the base to hold the pieces of sponge. Especially recommended was the inhaling tube, of the same size as the trachea, which allowed the patient to breathe through it freely and became "a continuation of the windpipe," as the different parts of the apparatus such as the stopcock, valves and mouthpiece, were all of the same dimension. The mouthpiece was of ebony but could be constructed of glass or earthenware. The all but inevitable nose spring, made of steel, completed the instrument. A second form of the inhaler was brought out as a table model. The bent tube for holding the ether, of the first design, was replaced by a glass urn mounted on a mahogany pedestal; but the essential parts of both models, including the mouthpiece, were the same. Both were reproduced in the April, 1847, number of the *Edinburgh Medical and Surgical Journal*, together with the inhalers of Squire and Startin.

Although Squire's inhaler was undoubtedly in demand, the administration of ether in London, as previously indicated, was largely in Robinson's hands during the first four or five weeks following the announcement of the discovery. This included both private and hospital practice, as well as a certain number of veterinary operations. Beginning with such painful procedures as the removal of decayed roots of previously extracted teeth, Robinson, using his modified inhaler, was soon giving ether for general surgery at the Metropolitan, King's College, St. Thomas's, Guy's and other hospitals. He apparently met with a considerable measure of success, although, as Sir Benjamin Ward Richardson<sup>45</sup> stated, the first inhalations of ether in England were "not so successful as to astonish all the surgeons, or to recommend etherization as a common practice." Here we have the echoes of Syme's pronouncements. Richardson's statement

\*The first surgical operation under ether in Ireland was performed by J. MacDonnell on January 1, 1847 at the Richmond Hospital in Dublin.<sup>40</sup>

might well have included some of the early trials of anesthesia in France and other parts of the Continent

In England distrust arose from the way in which the anesthetic was administered. It did not always take effect, and fatalities directly or indirectly attributable to the drug were reported. Liston himself was said to have lost much of his early enthusiasm for anesthesia. To offset these failures the administration of oxygen to resuscitate etherized patients began to be advocated. In accordance with this, Hooper equipped his large inhaler with a gas bag,<sup>46</sup> and by the end of March, 1847, Robinson was giving oxygen, following the administration of ether, as a routine procedure. John Snow at first took an active part in opposing the practice, to be revived later on.

Snow, who was the first physician to specialize in giving anesthetics and the author of the initial textbook on the subject, was six years Morton's senior. He served a long apprenticeship in his profession and was always a serious worker. He had received from the University of London the degree of Bachelor of Medicine in 1843 and that of Doctor of Medicine in 1844. He had engaged in various experimental studies on respiration and asphyxia, the results of which he had published, but he had failed to achieve any prominence. The ether discovery proved to be the turning point in his career.

Soon after the news of the discovery, and without any immediate thought of specialization, Snow carried out experiments on animals and on himself for which his previous work had prepared him. Richardson<sup>47</sup> records that the deciding factor in Snow's resolve to take up anesthesia was his chance meeting with a druggist of his acquaintance, who, carrying a large apparatus under his arm, informed him that he was getting into quite an ether practice, giving the drug "here, there and everywhere."

By January 23 Snow had perfected an inhaler. This instrument, as he acknowledged, was based on the principles of an inhaler brought out in 1842 by Julius Jeffrey, F.R.S., as an apparatus for the inhalation of "aqueous vapor." A contemporary description of Snow's inhaler, published in the *Pharmaceutical Journal*,<sup>48</sup> is as follows:

A round tin box, two inches deep, and four or five inches in diameter, with a tube of flexible white metal, half an inch in diameter, and about a foot and a half long, coiled round and soldered to it. There is an opening in the top of the vessel, at its centre, for putting in the ether and attaching the flexible tube belonging to the mouth piece. In the interior is a spiral plate of tin soldered to the top, and reaching almost to touch the bottom. When used, the inhaler is to be put in a hand basin of water, mixed to a particular temperature, corresponding to the proportion of vapour that the operator may desire to give, and the caps being removed, and the mouth piece attached, when the patient begins to inhale, the air gains the desired temperature in passing through the metal pipe, it then comes upon the surface of the ether, where it winds round three or four times before entering the tube going to the mouth piece, thus ensuring its full saturation, and preserving it at the desired temperature. [Snow usually maintained the temperature between 60 and 65° F.] There is no valve or

any obstruction to the air till it reaches the mouth piece, which is of the kind used in other inhalers and contains the valves necessary to prevent the return of the expired air into the apparatus.

With this instrument Snow asked to be allowed to administer ether at St. George's Hospital. He received permission to give it to out patients for tooth extractions, but when the success of his method had been observed for a day or two he was invited to administer ether for a surgical operation. This occurred on January 28, 1847, and shortly thereafter he was administering the drug regularly on operating days. He gave ether with almost unvarying success and soon made his appearance at University College Hospital, where Liston, struck by his quiet authority, took him by the hand. From that time he became the principal anesthetist in London.

Having chosen this field, Snow devoted himself to cultivating it, and the results of his painstaking investigations soon began to be published in a series of papers, appearing chiefly in the *Lancet* and the *Westminster Medical Gazette*, the majority of them having previously been read before the Westminster Medical Society, of which he had long been a member.

Snow's ether inhaler was reproduced in the *Lancet*, the *Pharmaceutical Journal* and other journals, first being shown in the *Lancet* of January 30, 1847. Although remaining basically the same, it underwent several alterations until it reached the form (Fig. 9) that is best known. A complete description of it occurs in Snow's first book.<sup>49</sup> "The round tin box" of the original design became one of "japanned tin or plated copper, of the size and form of a thick octavo volume." This box served as a water bath when the apparatus was in use, and at other times contained the elastic inhaling tube and facepiece. Snow's improved facepiece, enclosing both the nostrils and the mouth and permitting respiration as the patient might desire, dispensed with the rather formidable nose spring, which he termed "rude." The central part of the facepiece containing the valves was constructed of brass, tinned iron or plated copper, the rest was of thin sheet lead sufficiently pliable, like the mouthpiece of Robinson's inhaler, as to be easily adapted to the features. The lead was covered with silk or glove leather on its outer surface and lined with oil silk where it touched the face. The valves, of vulcanized rubber, were light and so constructed as to rise with the least pressure and close again of themselves, regardless of the position in which the patient was placed. The apparatus was made by Ferguson and later by Matthews, of Lincoln's Inn, and other instrument makers.

A strong advocate of the inhaling apparatus and the control that its use permitted, Snow had not altered his opinion when he published his book in September, 1847, the sponge having then been in use for six months. "The simple sponge is prefer-

able, for all cases, to many of the apparatuses which were in use," Snow<sup>50</sup> wrote, "but I cannot admit that it is equal to a good apparatus." He considered it an expensive method, since "not one half of the ether which is dissipated enters either the mouth or nostrils of the patient." He spoke of using five fluid ounces of ether in keeping an elderly patient insensible for more than two hours, but he ordinarily employed two or two and a half ounces in his in-

of a child and the administration of anesthesia obstetrics — long a controversial question — thereby firmly established

\* \* \*

Although bladders, either ox, sheep or pig, were frequently in use on the Continent and were advocated by Schuh, of Vienna, and others, the production of inhaling instruments quickly followed

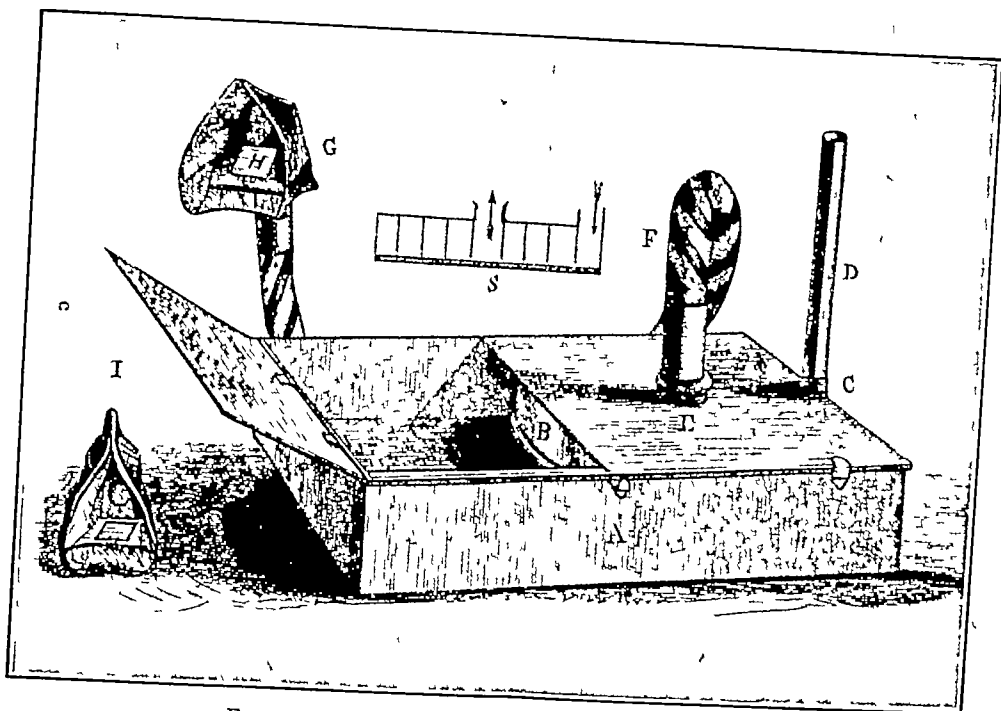


FIGURE 9 John Snow's Ether Apparatus (1847)

A is a box of japanned tin or plated copper, B, the spiral ether chamber of thin tinned brass or silver-plated copper, C, the opening in same for putting in and pouring out ether, D, a brass tube, five eighths of an inch in internal diameter, by which the air entered, which the patient inhaled, E, another opening in the ether chamber, F, an elastic tube about three feet long, G, the facepiece, H, the inspiratory valve, I, the same facepiece compressed to fit a small face, and S, a section of the spiral ether chamber

haler, which was approximately the amount used in most of the early instruments, although this varied somewhat with the age of the patient, children usually requiring less. While conceding that the sponge was the more suitable means in giving ether to infants, Snow used his inhaler with a small facepiece for children of two years and older. He conveyed the impression of not being especially in favor of rectal anesthesia, approved by Roux and first adopted by Pirogoff.<sup>51</sup>

With the introduction of chloroform Snow found his book, which had been well received, cast in the shade and turned to his studies of this new agent that he was later to administer, by handkerchief, to Queen Victoria on the important occasion (April 7, 1853) when she first accepted chloroform for the birth

the spread of anesthesia. Any attempt to catalogue them, however, would exceed the limits of this paper. The inhaler first employed by Velpeau, which had been designed by Joseph Charrière, of Paris, well known as an instrument maker, and the apparatus of Dieffenbach's, later reproduced in his monograph *Der Aether gegen den Schmerz*,<sup>52</sup> may be mentioned as perhaps two of the most important of these instruments.

Largely owing to the efforts of F. Willis Fisher, a Boston physician living in Paris, ether experiments in the French capital antedated those in London by several days, the initial demonstration in a Paris hospital going back to December 15, 1846, when Fisher was invited to administer the drug for an operation at the Hôpital Saint Louis, performed by

Jobert de Lamballe But the attempts to anesthetize the patient failed on this occasion, and other early experiments, including those carried out by Joseph Roux at the Hôtel Dieu and by Joseph-Francois Malgaigne at the Hôpital Saint Louis, which he reported at the French Academy of Medi-

with the anesthetic given by means of Charrière's inhaler and was regarded as a complete success<sup>54</sup>

Charrière's instrument — at once acclaimed in Parisian journals — was brought out in several forms, including a portable one His principal model at that time was a decanter-shaped glass bottle with

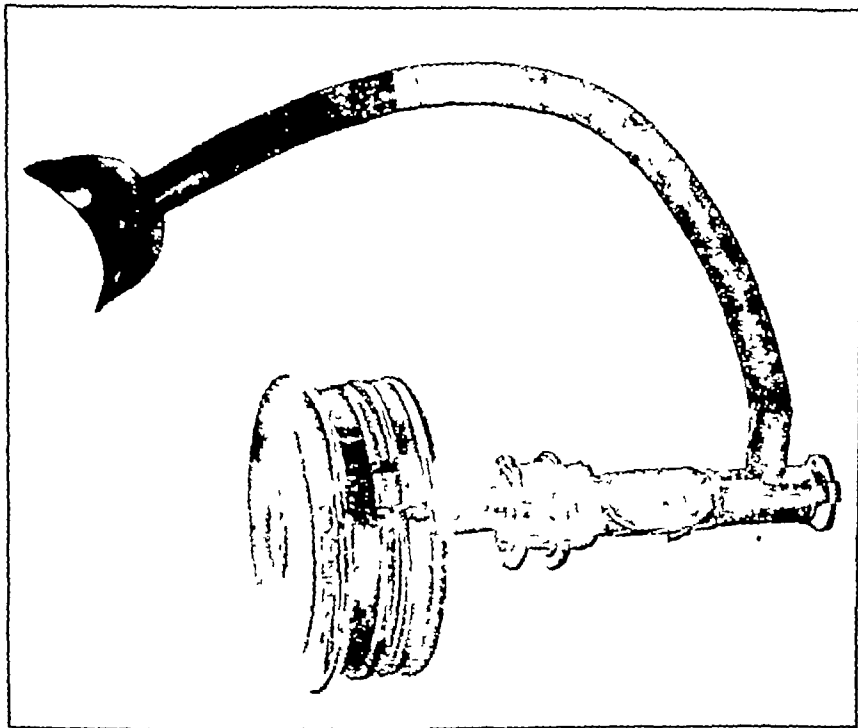


FIGURE 10 Luer's Inhaler (courtesy of the Massachusetts General Hospital)

The glass, cork-stoppered vessel is six inches in diameter with a depth of five and a half inches. In place of a sponge there is a four-and-a-half-inch cotton filter. The silk elastic inhaling tube is fifteen inches in length, with a circumference of three inches. The metal fittings and the mouthpiece, which is three inches long, with a depth of approximately one and a half inches, are apparently of lacquered brass.

cine on January 12, were only partially successful. This was apparently due to defective apparatus as well as a poor quality of ether.

The arrival of one of Morton's instruments, otherwise known as the Boston inhaler, about the middle of January did much to overcome the difficulties. Fisher,<sup>55</sup> to whom it had been sent, stated not only that he employed it in successfully administering ether but that it served as a model for all the Pansian instrument makers.\*

Velpeau, deterred by the previous failures, did not operate under ether until January 22, 1847. This operation, for tumor, took place at the Charité

an unusually wide base containing the ether saturated sponge cut and distributed in sections (Fig 11). He employed valves and the long flexible inhaling tubes so popular with the Europeans (Snow advocated one about three feet in length), as well as cork-padded nose pieces that were possibly a little lighter in their general form than the English variety. Early reproductions of Charrière's inhaler appeared in the January 26, 1847, issue of the *Gazette des Hôpitaux* and in the January 30 issue of the *Paris Gazette Medicale*. References to the instrument and its modifications continued to appear from time to time during 1847, principally in the *Gazette des Hôpitaux*. Charrière's inhaler also attracted favorable attention outside of France and was mentioned by Snow and Dieffenbach among others.

\*In the present collection of the Massachusetts General Hospital there are two interesting models of a glass inhaler (Fig 10) by Luer of Paris to record an additional apparatus which bears a certain resemblance to Morton's. Undated, they may belong to a later period but the construction of the flexible inhaling tubes and metal mouthpieces seems to relate them to the early inhalers.

In *Aether gegen den Schmerz*, published about seven months after Heyfelder<sup>55</sup> had performed the first surgical operation (January 24 1847) in which ether was employed in Germany, Dieffenbach gives evidence of his interest in apparatus. He mentions almost a dozen inhalers, including, in addition to Charrière's, Morton's, which he describes at some length, Robinson's and Smee's. His own instrument with its sponge-filled glass globe, was much like

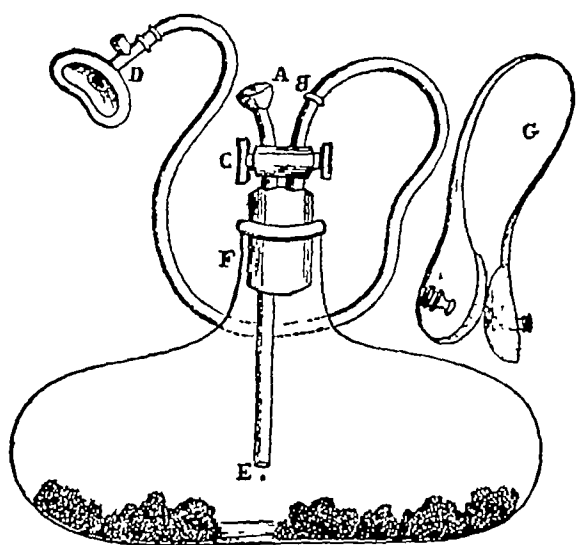


FIGURE 11 Charrière's Ether Inhaler (1847)

Air was introduced by the tube AE, which connected with the inhaling tube BD, terminating in a metal mouthpiece C indicates the valves, and G, the nose spring

Morton's inhaler, the chief difference being the long inhaling tube and the mouthpiece, formed like a shell and made of rubber or horn

Written from the viewpoint of the practical surgeon, Dieffenbach's monograph as a work on inhalation anesthesia was probably the most elaborate of its kind to appear at that time. His death occurred in November, 1847, when interest was beginning to shift to chloroform as an analgesic and when new and simpler apparatus for administering it were soon to be devised by Snow, Squire, Hooper, Smee, Charrière and many others. The ether inhalers that had not already been replaced by the sponge were for the most part set aside at about that date, to be revived, nevertheless, in the years ahead

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## HEALTH BILLS PENDING IN CONGRESS\*

## Part Three

FRANZ GOLDMANN, M D †

NEW HAVEN, CONNECTICUT

**I**N ADDITION to the National Health Bill, many other proposals are pending in Congress. They deal with construction of essential medical-care facilities, organization of health-service programs and promotion of medical research and professional education. Some of these measures are complementary to the National Health Bill, and some are alternatives to it.

## HOSPITAL SURVEY AND CONSTRUCTION BILL

*Description*

The Hill-Burton Bill, or Hospital Survey and Construction Bill (S 191), is designed to assist the states in surveying their needs for construction of necessary hospitals, developing programs to meet existing needs and building public and other non-profit hospitals in accordance with such programs.

To attain these objectives the adoption of a number of fundamental principles is proposed. A balanced program of hospitals and related facilities is to be developed throughout the country. It includes public-health centers, various types of hospitals — namely, general, tuberculosis, mental and chronic-disease hospitals and other types — and facilities such as laboratories, outpatient departments, nurses' homes and training facilities for nurses. Instead of calling for the building of federal hospitals, the bill proposes to assist the states in developing hospital programs, this assistance being confined to public and nonprofit hospitals and related facilities. The first step to be taken by the states would be a survey of all medical-care facilities within its boundaries. This inventory would be followed by the formulation of a state-wide building program. The project would have to be submitted to the federal authority in charge and, if approved, would be subsidized by federal grants-in-aid.

The number of beds to be provided under the terms of the bill is defined in detail. The total of general hospital beds for any state is not to exceed  $4\frac{1}{2}$  per 1000 population, except that in states having less than 12 and more than 6 persons per square mile, the limit shall be 5 beds per 1000, and in states having 6 persons or less per square mile,  $5\frac{1}{2}$  beds per 1000. The total number of beds for tuberculous patients is not to exceed two and a half times the

average annual deaths from tuberculosis in the state over the five-year period from 1940 to 1944, inclusive. The total number of beds for mental patients is not to exceed 5 per 1000 population and that for chronic-disease patients 2 per 1000. The number of public-health centers is not to exceed one per 30,000 population. It should be borne in mind that these figures refer to projects assisted by federal funds. To assure the building of qualitatively adequate hospitals the bill requires the formulation of general standards of construction and equipment for hospitals of different classes and in different types of location, the establishment by the states of minimum standards for the maintenance and operation of hospitals, state reports on the hospital situation, and approval of state plans. Of prime importance are the bill's requirements that adequate hospital facilities be available to all the persons residing in a state, without discrimination on account of race, creed or color, and that provisions be made for adequate hospital facilities for persons unable to pay for care.

Authority for the administration of the program is vested in the states and — what is most significant — in a single state agency as the sole agency responsible for both the survey and the administration of the hospital plan. At the federal level, the responsibility rests with the Surgeon General of the United States Public Health Service, whose administrative regulations and other functions are subject to the approval of the newly created Federal Hospital Council.

At the state as well as the federal levels advisory committees would be established. The state advisory councils are to include not only representatives of nongovernment organizations or groups and of state agencies but also of the general public. The Federal Hospital Council is to consist of the Surgeon General of the United States Public Health Service as chairman and eight members appointed by the Federal Security Administrator. Five of these members must be experts in hospital and health activities, and three will represent the consumers of hospital services. All appointed members of the council are to serve on a part-time basis. The council is authorized to appoint special advisory and technical committees.

The cost of both the survey and the construction program is to be shared by the federal government and the states. The bill includes an initial appropriation of \$5,000,000 for the surveys and a total of

\*This is the third of a series of four lectures on medical sociology given at the Harvard Medical School during February and March, 1946. They were sponsored by the Department of Preventive Medicine and were primarily intended for third year students.

†Associate clinical professor of public health, Yale University School of Medicine.

\$375,000,000 for construction purposes, to be spent over a period of five years. This money will be allotted to the states according to definite schedules. The states are to receive 50 per cent of their own expenses—but not less than \$10,000—for surveys and planning, and from one third to three fourths of their total expenditures for construction. The provisions of the measure are to be incorporated in the Public Health Service Act and thus become an integral part of the law governing the development and administration of health services under public auspices. The Hill-Burton Bill, as described, has been passed by the Senate and is being considered by a committee of the House of Representatives.

### *Advantages and Disadvantages*

For the first time in American history the development of a broad and balanced program of hospital and related facilities is under active consideration. If passed, the Hill-Burton Bill will put an end to the haphazard growth of facilities, with the resultant uneven distribution of all types of hospitals and the deplorable lack of certain special facilities. Due emphasis is placed on quantitative standards. The introduction of the approval system will serve not only to distribute the hospitals better but to improve their quality where indicated. The poorer states are to obtain relatively more financial aid than the wealthier ones. The administrative control is vested in the states, as it should be, and unification of the administration is proposed. The state advisory councils are composed of representatives of all groups concerned and are thus truly democratic. Enactment of the bill will influence the distribution of physicians and related groups, since it provides for the "workshops" so essential to the practice of modern medicine. The quality of medical care can be expected to improve in areas hitherto undersupplied with adequate hospitals.

The value of the bill in its present form is considerably impaired by several shortcomings. The measure does not contain provisions for the maintenance of hospitals and payment for professional services. It is satisfied with reasonable assurance on the part of states applying for grants that financial support will be available for maintenance and operation. To quote a hospital administrator who testified at the Senate committee hearing, "If people are too poor to build a hospital, they'll probably be too poor to run one." Adoption of the Hill-Burton Bill without the simultaneous passage of bills for the organization of payment for hospital and professional services will create serious problems in many areas. The danger of "ghost hospitals" must be avoided.

In vain does one look for a statement on the staffing of the hospitals. The nature of standards for the operation of hospitals is left to the states to determine. Is it not specified whether the hospitals

are to be open to all qualified physicians or to be restricted to some of them, whether they are to provide luxury services, or whether the physician will be permitted to charge unlimited fees. These are questions that require clear answers in the bill.

The proposals concerning the powers and functions of the Federal Hospital Council are contrary to the time-tested principles of sound public administration. Although composed of persons who devote nearly all their time to their private interests, the council has considerable authority, including the veto power, and important administrative functions. The Surgeon General of the United States Public Health Service and the Federal Security Administrator are made figureheads. Yet they are the very persons officially responsible to Congress and the public for the proper use of large sums of tax money. Such an administrative structure is utterly unsuitable. Councils composed of part-time members should exercise advisory functions only.

The bill fails to make reference to regional organization of hospitals. For years, experts in civilized countries have been contending that the pattern of hospital organization that was satisfactory in the nineteenth century has become obsolete in this age of rapid transportation. The future hospitals should be developed to serve regions rather than political units, a main hospital functioning as the center of an integrated system of district hospitals, rural hospitals and health centers.

Finally, the amount of money to be appropriated appears small, considering the immediate needs for replacement of obsolete buildings and additions.

### DENTAL-HEALTH BILL

Senators Aiken and Pepper have introduced a bill (S 1099) designed to amend the Public Health Service Act so as to provide assistance to states in developing and maintaining dental-health programs. The prevention, treatment and control of dental diseases are covered, as well as research in dental health care and pertinent educational projects. The program is to be financed jointly by the federal government and the states, along the lines followed in the past for health services assisted under the Social Security Act.

As it stands, the bill is too indefinite to warrant detailed discussion. Its main value lies in the fact that it directs attention to a sadly neglected field of health service, calls for the inclusion of preventive, therapeutic and educational services in one program, makes provision for research and professional education and proposes incorporation of organized dental-service plans in the Public Health Service Act.

### MATERNAL AND CHILD WELFARE BILL

#### *Description*

The Maternal and Child Welfare Bill (S 1318) is sponsored by Senator Pepper, and other senators,

including Senator Murray Its stated objective is to make more adequate provision for the health and welfare of mothers and children and for services to crippled children The bill is organized in three parts, covering maternal and child health services, services for crippled children and child welfare services

The maternal and child health services are made available to all mothers during the maternity period and to all children up to twenty-one years of age, regardless of income, race, creed, color, national origin and residence The program provides for complete health service, which is defined as follows

" medical, nursing, dental, hospital, and related services and facilities required for maternity care, preventive health work and diagnostic services for children, school health services, care of sick children, and correction of defects and conditions likely to interfere with the normal growth and development and the educational progress of children "

To promote quality of service, the state agencies are required to establish standards for professional personnel rendering medical, dental, nursing and related types of care or service and standards for hospital and other institutional care and services, to provide for adequate remuneration of professional persons and to furnish opportunities for postgraduate training

The patients are to have free choice of physician, hospital, clinic or health-service agency Payment to physicians participating in the program is to be on a per capita, salary, per case or per session basis or, in the case of consultations or emergency visits, on a fee-for-service basis The last-named method would therefore be the exception rather than the rule In line with principles established under the Social Security Act, approval of state plans is mandatory, and these plans must provide both for financial participation by the state and for a program effective in all parts of it

The proposed service would be financed jointly by the federal government and the states The bill makes an initial appropriation of \$50,000,000 for payments to states that have submitted approved plans for developing such programs and providing such care and service, and it defines in detail the schedule for the allotments to the states The United States Children's Bureau is to have administrative responsibility at the federal level and is aided by federal advisory committees State agencies are to be the heart and center of the proposed administrative organization, and they are to be assisted by general advisory councils, composed of representatives of the public as well as of the professions and agencies and by technical advisory committees

The services for crippled children are to be expanded by adoption of the same basic policies as those proposed for the extension of maternal and child health services The initial appropriation for grants to ~~the~~ set at \$25,000,000

The child-welfare services are designed to curb delinquency, and their extension is to be financed by an initial appropriation of \$20,000 000

### *Advantages and Disadvantages*

A bill dealing with maternal and child health service is certain to find a sympathetic response As Sir George Newman once wrote, "The safeguarding and nurture of motherhood and child life must be a first requirement in the building of any nation " What, then, are the relative merits of the health provisions of the Maternal and Child Welfare Bill?

The measure would make service available to everyone without discrimination, provide for completeness of service and develop the program gradually over a ten-year period so as to stimulate the improvement of standards as well as of essential facilities and services These are highly commendable features But the bill also has many weak points

The health provisions of the bill are a halfway measure, since one age group and one condition — maternity — are singled out The family is divided, and this is contrary to the basic principle of serving the family as a unit The demarcation by age is artificial and poses intricate administrative problems The people to be served will wonder why a married woman gets medical care when she is pregnant but not when she is sick, and why persons older than twenty-one are excluded It would be wiser to concentrate on the passage of a health bill designed for both children and adults and covering all health conditions

There is little in the bill concerning the organization of professional services No definition of professional personnel is given, in contrast to the National Health Bill, which clearly states that licensed physicians, dentists and nurses shall be qualified to render service Does this omission imply that nonmedical practitioners can expect to be admitted? The term "group practice of medicine" does not appear in the bill This is all the more regrettable because effective child-health service requires organized teamwork by specialists and general practitioners

The funds for the support of the program are to be obtained by general taxation This raises the old question of the relative merits of general taxation and insurance<sup>1</sup> In deciding on the future policy utmost care should be taken to avoid the establishment of two systems of raising funds for the support of services for self-supporting people.

The sum to be appropriated is extremely modest, to say the least. The amount of \$50,000,000 for distribution to the states in the first year exceeds the allocations for the program for the wives and infants of enlisted men (EMIC) by only \$7,000,000 It is hard to see how a program for all the mothers and all the children in the country can be operated

with the funds suggested, even if the birth rate should decline in the years to come

### THE NATIONAL MENTAL HEALTH BILL

The National Mental Health Bill (HR 4512), introduced by Representative Priest, supersedes an earlier bill, the National Neuropsychiatric Institute Act. Its objective is to amend the Public Health Service Act to provide for research relating to psychiatric disorders and to aid in the development of more effective methods of prevention, diagnosis and treatment of such disorders. The term "psychiatric disorders" includes diseases of the nervous system that affect mental health.

To carry out these purposes the bill proposes the authorization of four important policies. These are the allotment of grants-in-aid to universities, hospitals, laboratories and other public or private institutions and to individuals for such research projects as are recommended by the newly established National Advisory Mental Health Council, the construction and equipment of buildings and facilities to be known as the National Institute of Mental Health, which is to be part of the National Institute of Health, the admission and treatment at the institute of voluntary patients as well as patients of St. Elizabeth's Hospital, in Washington, D. C., and the development of training and instruction in matters relating to the diagnosis, prevention and treatment of psychiatric disorders. Although nongovernmental institutions would play a large role in education and research, the National Institute of Mental Health would serve as a focal point for research, experimentation and advanced or specialized training, and as a clearing house for the collection and dissemination of information concerning advances in the prevention, diagnosis and treatment of psychiatric disorders.\*

This program is to be administered by the Surgeon General of the United States Public Health Service at the federal level and by state mental-health authorities at the state level. The National Advisory Mental Health Council, consisting of the Surgeon General and six members, is created and is charged with the review and recommendation of research projects, the collection and publication of information on studies in the field of mental health and the recommendation of grants for training of personnel.

The bill proposes an initial appropriation of up to \$4,500,000 for the building and equipment of the new institution and of a total of \$11,000,000 for the current expenses of the program during the first year.

In December, 1945, the House committee reported favorably on the bill with the amendments.

There can be no doubt that this legislative proposal is a step in the right direction. One can only express the hope that it will be enacted and soon be followed by a bill for the improvement of facilities and services for persons with mental deviations. In

many parts of the country such a service program lags behind the present knowledge of mental deviations and the methods for their proper treatment.

### NATIONAL INSTITUTE OF DENTAL RESEARCH BILL

The National Institute of Dental Research Bill (S 190), introduced by Senator Murray, is designed to provide for, foster and aid in co-ordinating research relating to dental diseases and conditions and to establish the National Institute of Dental Research. It authorizes federal grants-in-aid to the states for research in the prevention and control of dental diseases and conditions, as well as the establishment of a federal institute as part of the National Institute of Health, which will serve as a central research and training institution and a co-ordinating agency. Closely following the lines of other health bills, the measure vests the Surgeon General of the United States Public Health Service with administrative responsibility and creates the National Advisory Dental Research Council to review research projects, collect and publish pertinent information and review applications for grants-in-aid.

The initial appropriations for this program include up to \$1,000,000 for the building and equipment of the institute and \$730,000 for each fiscal year to cover the current expenses of the program.

Everyone who has carefully studied the many earlier surveys of mouth conditions and the recent findings made in connection with the Selective Service examinations is aware of the magnitude of the dental-health problem and will lend support to any proposal for intensive research. This purpose, however, is not served by the offer of several dissimilar proposals in different bills. There appears to be need for agreement on the policy to be pursued, as well as for concentration of legislative effort.

### NATIONAL SCIENCE FOUNDATION BILL

The National Science Foundation Bill (S 1720), introduced by Senator Kilgore, is a compromise bill succeeding the earlier Kilgore Bill (S 1297) and the Magnuson Bill (S 1285). One of its objectives is to advance the national health and welfare, and its general policy is clearly stated in the following words: "Full development and application of the Nation's scientific and technical resources is essential for the national health and welfare."

Use of tax funds for the support of research by both governmental agencies and nongovernmental organizations is the core of the proposal. Of the total funds not less than 15 per cent are to be expended for research and development in health and medical sciences. These allocations are to supplement rather than supplant the functions or activities of other governmental agencies authorized to engage in scientific research and development. They are to be made for projects approved by the administrator and undertaken on behalf of the

National Science Foundation Freedom of research and publication is assured by the provision that every effort is to be made to eliminate restraints on the free expression of scientific views and to ensure full freedom in the exercise of creative talents, in the development of new ideas and in the method of research. Any person engaged in such research and development activities is not precluded from discussing, writing or publishing his own findings and conclusions.

In addition to research, undergraduate and postgraduate education would be supported by tax funds. The bill contemplates an authorization to award scholarships and fellowships to persons for scientific study or scientific work at nonprofit institutions of higher education or other institutions, selected by the recipient of such aid, for such periods as the administrator may determine, in the United States or in foreign countries. With this the door to medical education is opened to many qualified students lacking the necessary financial resources.

To administer this program, the creation of a special central agency, the National Science Foundation, is proposed. This agency has a divisional structure and includes eight divisions, one of which is the Division of Health and Medical Sciences. The Interdepartmental Committee on Science is to correlate and appraise research activities of all federal agencies engaged in or concerned with this field.

Full-time administration of the foundation is the guiding principle of organization. A full-time administrator is to be appointed by the President by and with the advice and consent of the Senate. There is to be a full-time deputy administrator, appointed by the President, and full-time divisional directors and staff members, all appointed by the administrator. The National Science Board of nine members is established to advise the administrator on all matters of major policy or program or budget, and divisional scientific committees of not less than five and not more than fifteen members will serve the divisions in an advisory capacity. The members of the board, the divisional committees and the staff of the foundation are to be chosen without regard to their political affiliations and solely on the basis of their demonstrated capacity to carry out the purposes of the foundation and their fitness to perform the duties of their office.

The Kilgore Bill expresses the best scientific thinking, is drawn in conformity with the wishes of those interested in the promotion of unhampered research and deserves enactment. It has been passed by the two Senate committees concerned.

#### RESEARCH PROVISIONS OF THE NATIONAL HEALTH BILL

The National Health Bill, or Wagner-Murray-Dingell Bill, in Title I includes research and the performance of demonstrations in the definition of public-health work, declares demonstrations to be part of the maternal and child health program and

the services for crippled children, and requires the United States Children's Bureau to make and aid in the financing of such studies, demonstrations, investigations and research as will promote the efficient administration and operation of this part of the bill.

Title II, which deals with prepaid personal health service benefits, contains the following important section:

For the purposes of encouraging and aiding the advancement and dissemination of knowledge and skill in providing benefits under this Act and in preventing illness, disability and premature death, the Surgeon General is hereby authorized and directed to administer grants-in-aid to nonprofit institutions and agencies engaging in research or in undergraduate or postgraduate professional education.

It is indeed gratifying to find so much emphasis placed on research, but it is disturbing to notice the absence of an over-all plan to correlate the various provisions scattered in many bills.

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This presentation, intentionally limited to some of the major bills introduced in 1945, shows that there is a wave of enthusiasm for health legislation. Porter R. Lee<sup>3</sup> once wrote "The crystallizing of enthusiasm into programs is a wholesome development. It betokens an awakened community alert to its social obligations, and an awakened community is a bulwark of progress. Moreover, concepts, ideals and enthusiasm are of little effect until they do crystallize into programs." We find ourselves in a situation that resembles what Voltaire called the "*embarras de richesse*" (the embarrassment of riches).

In deciding on the various legislative proposals, we are faced not so much with the problem of rejecting obviously inadequate measures as with the hard choice between good and better plans. Let us keep in mind that long-term strategy, rather than stop-gap tactics, assures ultimate victory in the fight against disease, defect, human suffering and poverty. The question to be answered may be formulated as follows: Do we want piecemeal legislation, with its inevitable result of fragmentary and unequal development, or comprehensive health legislation, with its promise of substantial achievements throughout the country? The issue is well stated in a recent report of the United States Public Health Service: "The Nation cannot afford to be content with less than a comprehensive program — a program to apply throughout the length and breadth of the land, in every community, all the knowledge we have for prevention of disease, the relief of suffering and the promotion of health."<sup>4</sup>

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## MEDICAL PROGRESS

### NORMAL GROWTH AND DEVELOPMENT DURING ADOLESCENCE (Concluded)\*

HAROLD C. STUART, M.D.†

BOSTON

#### ADOLESCENT CHANGES IN PHYSIOLOGIC FUNCTIONS *Basal Metabolism*

There is of course an increase in the number of basal calories consumed per hour by the body as it increases in size year by year, and this is greater during pubescence than previously because the body size is increasing more rapidly. There is, however, less clear evidence regarding any fundamental increase in the basal metabolic rate associated with pubescence that is not explained on the basis of increased amount of active protoplasmic tissue.

In a comprehensive study of basal metabolism in girls, Talbot, Wilson and Worcester<sup>45</sup> in 1937 investigated the effects of pubescence on these rates. They concluded from a review of all data that an elevation of the heat production of girls tends to start at about ten years of age and reaches its maximum at the menarche, but that this rise is not a constant finding and that puberty per se cannot be considered the causative factor. They believed that there was sufficient evidence that the increased rate of growth in height during this period was the primary factor. Nylin<sup>46</sup> expressed the same opinion in 1935. Shock<sup>47</sup> has presented a curve for the basal heat production of girls in relation to the menarche, expressed as calories per square meter of surface area per hour. This shows a slight rise in the two and a half to three years before the menarche, an absence of change to the menarche and a continuing decline during the first three years thereafter. This period of rapid fall is more closely associated with the menarche than with any particular age. Webster, Harrington and Wright<sup>48</sup> report thorough longitudinal studies of basal metabolism in a few boys and girls over these years and discuss the changes in relation to growth and development. Johnston<sup>49, 50</sup> made closely repeated determinations of metabolic rates in girls during the year of the menarche. He found them markedly unstable at this time, with a tendency to high rates just before the menarche and lower rates shortly after it.

Lewis and his associates<sup>51, 52</sup> have conducted extensive longitudinal studies of basal metabolism in children up to fifteen years of age and have provided valuable tables of norms for sex and age. They failed to establish any absolute increase during

pubescence in the mean basal metabolism expressed as calories per square meter per hour. They point out, however, that during the ages of eleven to fifteen years in boys and ten to twelve years in girls, the rate of fall is greatly diminished in comparison with that in the preceding years, being only one quarter of the earlier rate in boys and one half of it in girls. They interpret this as indicating a relatively increased metabolism during pubescence. Talbot and his associates<sup>45</sup> considered the possibility that the enlargement of the thyroid gland that often occurs at this time might be responsible for an increased metabolic rate, but they concluded that the evidence does not point to any such relation. They found no trend toward an elevated pulse rate at this period that could account for an increased metabolic rate, but Shock has since reported a rise of ten points in the average pulse rate in girls during the pubescent period.

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There appears to be some disagreement on the question whether the basal metabolic rate is most advantageously expressed in terms of surface area, height or weight. Talbot<sup>53, 54</sup> recommends that it be expressed in terms of urinary excretion of creatinine. His reason is that this excretion is a function of the amount of muscle in the body and that muscle is the principal active protoplasmic tissue. Since it is peculiarly difficult to interpret basal metabolic rates during adolescence because of the great normal variability and the many factors concerned in determining any given rate, it seems especially desirable to use several methods of expression and to consider the values obtained by each method in respect to appropriate norms. So far as possible the develop-

\*From the Department of Maternal and Child Health, Harvard School of Public Health, the Department of Pediatrics, Harvard Medical School, and the Children's and Infants' hospitals, Boston.

†Professor of maternal and child health, Harvard University, head of Department of Maternal and Child Health, Harvard School of Public Health, visiting physician, Children's and Infants' hospitals.

mental age should be taken into account as well as the chronological age. The various tables of values published in the references cited are especially useful for this purpose.

Although the evidence concerning the nutritional requirements during the adolescent years is not reviewed in this report, it is of interest to call attention to the changes in the caloric values of the diets consumed by adolescents during the years in which the basal consumption is changing in the manner described.

If one considers the basal calories in relation to total caloric intake at the beginning and at the end of pubescence, a suggestion is given of the differences between boys and girls at these periods in muscle mass, which primarily determines normal basal calories, and in physical activity, which is one of the major variables that contribute to the differences between basal and total calories. The tables presented by Lewis<sup>8</sup> show that for girls of ten to eleven years of age the average caloric consumption per hour is 493, or 1183 a day. Wait and Roberts<sup>55</sup> estimate that at ten years the average total caloric intake of girls is 2100. Lewis's tables give values for average basal calories for boys of twelve to thirteen years as 53.5 an hour or 1284 a day, and the best estimate of total caloric intake for boys at twelve years appears to be 2600 calories. Thus, at the age of onset of pubescence, when body size is much the same in both sexes, the basal caloric consumption of boys is about 10 per cent greater than that of girls, whereas the total calories taken are nearly 25 per cent greater. The same data for the end of pubescence are as follows. Between the ages of thirteen and fourteen the basal caloric consumption of girls is given as 56.5 an hour or 1356 a day, and the total calories consumed at thirteen years as approximately 2600. The corresponding figures for boys aged fifteen to sixteen are 64.0 an hour or 1536 a day, and the total calories at fifteen years in the neighborhood of 3500. Thus, at a comparable stage of late pubescence, but with boys on the average considerably larger than girls, the basal caloric consumption is nearly 15 per cent greater in boys than in girls and the total calories consumption is about 25 per cent greater.

Wait and Roberts found that the largest increase in the average total caloric intake occurred in the thirteenth year, during which the average girl is accomplishing her maximum growth. These authors call attention to the great variability both in the number of calories consumed by children of the same age and in the day-to-day intakes of the same children. When one considers that caloric needs are principally determined by basal needs, together with the amount of muscular activity, and that basal needs are largely influenced by size and particularly amount of muscle, these age and sex differences are quite understandable. They should all be taken into account both in interpreting basal metabolic

rates and in considering dietary needs during the adolescent years.

#### *Calcium and Nitrogen Retention*

Johnston<sup>56</sup> has published several studies of calcium and nitrogen retention during the adolescent years under various circumstances. In this connection he has brought out several interesting relations between glandular activity, appetite and growth. High retention of calcium and nitrogen tend to occur just before the menarche and a sharp fall takes place immediately thereafter. This rise and this fall, however, sometimes precede and sometimes follow the first period. Estrogenic substances administered to normal girls at puberty depress calcium balances and occasionally nitrogen balances as well. Johnston concluded from studies of normal and abnormal thyroid function and thyroid therapy during adolescence that optimum retentions of calcium and nitrogen occur when metabolic rates are elevated within the normal range but not excessively stimulated.

#### *Other Physiologic Activities*

Most of the physiologic processes that are unassociated with sexual development or with the basic endocrine activities related to sexuality have become well stabilized before adolescence, and relatively small changes take place in them during the latter years of growth.

Shock<sup>47</sup> has obtained physiologic data based on studies of 50 girls every six months from the ages of twelve to eighteen years, with the age at the menarche known, and has plotted them on a menarcheal-age basis. These include pulse rates, systolic and diastolic blood pressures and pulse pressures, and basal respiratory volumes. His studies show that on the average among girls the systolic blood pressure rises steadily during the three years preceding the menarche — from 97 to 107 mm — and remains at about the latter level during the ensuing five years. The diastolic pressure shows no constant change during either period. Hence, there is a net increase in pulse pressure during the premenstrual period, with little change thereafter. The average pulse rate shows a rise from 63 three years before the menarche to 73 one year before it and a slight drop to 70 at the menarche. The pulse falls further to 65 in the first three years and to 60 in the next two after the menarche. The basal respiratory volume expressed as liters per minute rises sharply in the two or three years before menarche — from 3.2 to 4.7 liters — and remains constant thereafter, but expressed as liters per square meter of body surface area per minute it presents an early rise followed by a gradual fall. Thus, in all these measurements except diastolic pressure there appears to be an increase during pubescence in girls.

In another publication, Shock<sup>57</sup> presents norms for 50 adolescent boys and 50 adolescent girls on a

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HAROLD C STUART, M D †

BOSTON

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\*From the Department of Maternal and Child Health, Harvard School of Public Health, the Department of Pediatrics, Harvard Medical School, and the Children's and Infants' hospitals, Boston.

†Professor of maternal and child health, Harvard University, head of Department of Maternal and Child Health, Harvard School of Public Health, visiting physician, Children's and Infants' hospitals.



since growth does not occur and that with excess excretion general uniform overgrowth takes place

The initial stages of sexual differentiation, especially of the growth of the gonads, are believed to result from an increased production of the gonadotropic and adrenocorticotrophic hormones, the former probably acting directly and the latter indirectly by stimulating the androgenic zones of the adrenal glands. Lack of these hormones during the prepubescent period results in some degree or type of hypogonadal state. An excess of these hormones prior to puberty produces manifestations of precocious sexual development, with or without early reproductive capacity. Some of these deviations from the normal may also occur as a result of abnormal levels of secretion of the specific part of the adrenals referred to, owing to disease in these glands.

The gonadotropic hormone is excreted in the urine, and repeated quantitative determinations have been made throughout adolescence on twenty-four-hour specimens of urine in several groups of normal boys and girls. The reports of Nathanson, Towne and Aub<sup>66</sup> on studies at Harvard and of Dorfman, Greulich and Solomon<sup>67</sup> on studies at Yale are of particular interest. These indicate that the gonadotropic hormones — measured by Nathanson as the follicle-stimulating hormone (F S H) and by Dorfman as gonadotropin — do not appear in measurable quantities in girls until eleven years of age or in boys until thirteen years. Excretion of the hormones increases rapidly in amount after their first appearance, and this increase coincides with the dramatic increase in the hormones from the peripheral sex glands. Nathanson et al point out that the secretion of the follicle-stimulating hormones probably precedes that of the gonads, but that the methods available for their assay at the time of the study were not sufficiently precise for their presence to be recognized in their initial small concentrations.

Estrogens are the female sex hormones, which are probably produced both by the adrenal glands and by the ovaries, and androgens are the male sex hormones, measured as the 17-ketosteroids and produced both by the adrenal glands and by the testes. According to Nathanson, Towne and Aub, estrogens and androgens are both present in both sexes in fairly constant but negligible amounts between three and seven years of age. The amounts of these excreted in the urine increase moderately and to a like degree in girls and boys between seven and nine years, the 17-ketosteroids on the average being slightly higher in boys and the estrogens in girls. Between nine and eleven years the 17-ketosteroid excretion increases more rapidly in boys and the estrogen excretion in girls, but individual differences are extremely wide. During the twelfth year on the average, but sometimes earlier, a cyclic variation in output of estrogens by girls becomes obvious, with wide differences between the peaks and minimum

values in single cycles. The average values continue to rise in girls after eleven years, whereas the output of estrogens by boys remains relatively constant. During this same period boys excrete increasing quantities of the 17-ketosteroids, but the difference between the sexes in the excretion of androgens is not nearly so marked as that of estrogens becomes.

Nathanson and his co-workers conclude that there is a primary stimulation of the gonads and adrenal glands that causes a steady — noncyclic — increase in both androgens and estrogens in both sexes. The high values and cyclic excretions of estrogens occurring in girls result from a superimposed stimulation — presumably of the ovaries by the pituitary gland after the former have matured sufficiently to excrete quantitatively. Similarly, the high urinary values of the 17-ketosteroids occurring later in boys are thought to be the result of an added excretion from the maturing testes. Thus, the gonadotropic hormones of the pituitary apparently first stimulate the adrenal cortex to increased but steady excretion of 17-ketosteroids and estrogens. At the same time they stimulate the growth and maturation of the testes and ovaries and later stimulate these organs to hormonal activity. This causes a higher but relatively steady excretion of androgens by boys and a much higher and cyclic excretion of estrogens by girls, thereby leading to the ultimate marked differences between the sexes in the amounts of these hormones found in the urine.

Talbot et al<sup>68</sup> have also studied the excretion of 17-ketosteroids in relation to age and have emphasized that the amounts recoverable from the urine before ten years are negligible. They also found that little sex difference is discernible until fifteen years of age and that the output by boys increases up to eighteen years of age at least. It should be pointed out, however, that it has not been demonstrated that the gonads themselves secrete any hormones that affect the development of the sex organs or sex characteristics prior to the pubescent period. Moore<sup>69</sup> has reviewed the evidence relating to the gonads during embryonic and prepubescent life, and concludes that they do not secrete hormones that affect sex-organ development during these periods. In considering the relations between the levels of these excretions and the physical changes associated with adolescence, the following observations have been made. First, the simple linear elevations in these excretions have progressed for several years, probably three or four, before the first clinical signs of sexual differentiation appear. This covers the period that I have referred to as prepubescence. Second, the sudden sharp rise of estrogens in girls, which precedes by a short interval the development of cyclic variations, is closely associated with the early physical changes of pubescence and rapid growth of the ovaries and may be said to mark the beginning of the pubescent period. Cyclic variations in excretion of estrogens are apparently taking place

chronological-age basis from eleven and a half years to seventeen and a half years. The principal sex difference appears to be that after fourteen years of age the average systolic pressure and pulse pressure are considerably higher for boys than for girls. Graham<sup>58</sup> also presents figures for blood pressures based on repeated determinations in 3580 children, from which he secured modal values as well as variability values with age. Variability tended to increase with age but was more pronounced among girls between ten and thirteen years old than among boys of the same age range. The tables presented by Richey<sup>59</sup> giving blood-pressure values by age also serve as useful reference standards. Graham reviews the relations between blood-pressure levels, body size and physical maturation.

The changes in blood cytology have been studied by Osgood and Baker<sup>60</sup> up to thirteen years and by Mugrage and Andresen<sup>61</sup> for the same period. These changes are not of sufficient magnitude to deserve description here, but the tables presented by these authors serve as valuable reference standards for the early years of adolescence. The values given for thirteen years appear to be near the adult values for women, although the hemoglobin and red-cell values are somewhat below those for men.

#### THE ENDOCRINE GLANDS

It has been recognized for many years that the processes of growth and maturation are influenced by, if not completely under the control of, hormones secreted by several of the endocrine glands. Extensive research during recent years, based largely on animal experimentation but supplemented by studies of grossly abnormal children and the clinical use of endocrine products, have done much to clarify understanding of the mechanisms involved. More recently the development of methods for determining the amounts of certain hormones excreted in the urine of normal as well as of abnormal children has especially helped to confirm certain hypotheses regarding the endocrine activities associated with growth and maturation during adolescence.

It is not within the scope of this report to review the extensive literature in this field. The reviews prepared by Aldrich<sup>62-64</sup> several years ago are still useful for background. There is now in press a clinical review by Talbot and Sobel<sup>65</sup> that considers the more recent evidence concerning the endocrine factor, as well as other factors that determine growth. A few recent studies of the urinary excretions of certain hormones by normal children year by year during adolescence are so pertinent to the subject of this report that the findings will be reviewed.

The glands known to be involved in the developmental changes occurring during adolescence are the thyroid, the pituitary, the adrenals and the gonads. The thyroid gland is included because of its known relation to basal metabolism and to osseous development and because there is a tendency for

it to hypertrophy during adolescence. The participation of the thyroid in the complex glandular interrelations that constitute the mechanism controlling adolescent development does not, however, appear to be a major or direct one. It has been pointed out that the differences in basal oxygen consumption, which should reflect changes in thyroid activity, are primarily related to body size and muscle mass and that age differences in basal metabolic rates corrected on this basis are not consistently different to any significant degree. The determination of blood iodine levels as an index of thyroid activity appears to have value principally in dealing with diseased persons. In some series of reported cases considerable enlargement of the thyroid gland has been found to occur during pubescence in a large proportion of cases, but this does not appear to be uniformly true in all localities. Pryor<sup>66</sup> examined 74 girls in San Francisco at the time of onset of the menses and reported slight enlargement in 16, moderate enlargement in 47 and definite lateral enlargement of both lobes in 10, with only 1 girl showing no enlargement. I have, however, found enlargement in only a small proportion of the children studied in Boston, and in these cases it was of slight degree.

The relation of the thyroid gland to epiphyseal growth and the steps leading to union with diaphyses is well known. The rate of maturation in these locations is unquestionably influenced by the drug thyroid, and normal thyroid function is necessary for normal osseous development. The pituitary and possibly other glands play a part in regulating this process, and its continuance to the point of union of epiphyses with diaphyses ultimately leads to the cessation of growth. It does not, however, appear that any sudden change in thyroid activity is responsible for the termination of growth or for any of the specific changes associated with pubescence or post-pubescence.

The glands that are of special interest in this connection are the pituitary, the adrenals, the ovaries and the testes. The interactions of the hormones elaborated by these glands appear to be responsible, in large measure at least, for the progressive stages of adolescent development that have been described. The anterior lobe of the pituitary gland is known to elaborate several hormones, among which the growth hormone, the gonadotropic hormone—of which there are two or more fractions, follicle-stimulating and gonadotropic—and the adrenocorticotrophic hormone have been most thoroughly studied. It appears that an increased secretion of the growth hormone is primarily responsible for the general acceleration of the rate of growth of the body as a whole and that a decrease in this secretion, probably brought about by action of the gonads, accounts in part for the sudden deceleration in growth. This conclusion is based primarily on studies showing that in its ab-

some deviations in physical status or growth progress. A carefully taken family history often makes it appear that these are intrinsic in nature, but this conclusion cannot be accepted until a careful investigation of environmental factors has been carried out and a serious effort has been made to correct unfavorable influences. It is also unsafe to compare two racial groups of children and to conclude that any differences found to exist between them are racial in origin. Several recent studies offer strongly suggestive evidence that dietary habits or factors associated with socioeconomic circumstances may have more to do with the differences found to exist between racial groups than has the factor of race itself.

Some writers have stressed the differences in size and build and rate of maturation between groups of children living under different climatic conditions, but here again one must be cautious in accepting climatic factors as responsible unless racial differences on the one hand and socioeconomic differences on the other have been taken into account. Mills<sup>74</sup> has brought together considerable evidence in support of a climatic effect. This evidence deals not only with the average age of the menarche and with the rates of growth of children in different climates but also with these differences in animals reared in different atmospheric conditions. Mills states that in regions of depressing moist heat, both growth and the menarche are delayed and the final adult form is slender and small, whereas growth and pubescent development are most accelerated and the most robust body forms are seen in the stimulating, stormy temperate regions. He has obtained exactly similar differences in laboratory animals, where ease or difficulty in loss of body heat was the experimental variable.

Michelson<sup>75</sup> has attempted to determine whether differences in the age at the menarche between Whites and Negroes are attributable to race or socioeconomic circumstances. He studied twelve separate population groups and showed that Negro girls born and living in the West Indies reached the menarche on the average at 13.99 years, those in the southern part of the United States did so at 13.68 years, those in New York State at 12.94 years, and a small well-to-do group in New York State at 12.85 years. White girls born and living in New York State reached the menarche on the average at 12.86 years. Although the average age at the menarche for all Negroes is considerably later than that for Whites, this breakdown into groups makes it seem extremely doubtful that race per se is primarily responsible.

Other students have reported differences in menarcheal ages for different socioeconomic groups, with very late occurrence among girls in the less favored groups. Larger samples and better selected groups must be studied, however, before the influence of socioeconomic factors can be considered to have been established. The same may be said

of the recent reports from Europe to the effect that girls are now menstruating about one year later than was previously usual in countries subjected to severe dietary restrictions and other socioeconomic stresses during the recent war. The accumulating evidence suggests strongly, however, that prolonged undernutrition, especially in calories and protein, may retard maturation as well as physical growth. This is not surprising in view of the fact that chronic starvation leads to amenorrhea in women and to loss of the secondary sex characteristics in both men and women.

Meredith<sup>76-78</sup> has reviewed the evidence concerning the effects of race, region and socioeconomic factors on the height and weight of children. Using the Harvard Growth Study data, he compared children born and living in Massachusetts of North European ancestry with those of Italian ancestry in respect to stature. The former exceeded the latter at all ages from seven to seventeen years in both sexes. The increments of gain year by year were not significantly different during this period, however, the racial difference having been established by seven years, the earliest age studied.

In another study based on more than 60 samples of boys between the ages of nine and fourteen years representing differences in race, class, time and region, Meredith found that boys in the United States of various ethnic groups, otherwise roughly comparable, differ in average height between groups up to a maximum of 5 cm, that white boys residing in different parts of the United States vary little in average height and weight, and that white boys of the professional and major managerial classes are taller and heavier than those of the unskilled and semiskilled classes, the differences not exceeding 3 per cent for stature and 6 per cent for weight.

Meredith's most interesting findings have to do with a striking secular trend over the last fifty years. His analysis of the measurements obtained in Toronto school children in 1892, 1923 and 1939 are of particular interest. The typical Toronto boy aged thirteen to fourteen years was taller in 1939 than was the boy of 1892 by nearly 9 cm, and the typical boy of 1923 was about midway between. The differences at all ages were in the same direction, although of less marked degree. Meredith also finds that boys in the United States today, both White and Negro, are 6 to 8 per cent taller and 12 to 15 per cent heavier than were boys half a century ago. In general, secular differences in the United States covering the last half-century are twice as large as any of the other differences considered, whereas geographical differences are the smallest of all. Several studies of the heights of college boys in recent years and of their fathers while in college, and similarly of college girls and their mothers a generation ago, have revealed a considerable increase indicative of a secular trend. The causes for these evidences of increasing size with time call for further

during much of the pubescent period in girls — that is, for a year or more prior to the menarche. It is therefore consistent with these occurrences to postulate that the ovarian follicular hormone is necessary before cyclic excretions can begin, and that under this stimulation uterine development must have progressed sufficiently before the menstrual cycle can be completed. The menarche thus follows a period of several years of gonadal endocrine development. Third, the first sharp increase in the excretion of 17-ketosteroids in boys is associated with rapid growth of the adrenal glands and precedes that of rapid growth of the testes. A further increase is associated with rapid growth of the testes and appearance of the secondary sex characteristics. This association of events lends support to the presumption that the former is primarily of adrenal origin and the second of testicular origin. Lastly, the shift from neuter configuration to greater differentiation in physical characteristics accompanies the changes in the levels of these hormonal excretions. Nathanson and his associates<sup>70</sup> have reported a correlation of 0.8 between excretion of 17-ketosteroids and that of urinary creatinine in both boys and girls. Since the latter is a function of muscle mass, androgenic excretions are presumably closely correlated with amount of muscle. The greater development of muscles in boys over girls actually occurs during the years when the excretion of androgens is becoming markedly greater in boys than in girls. Both Nathanson and Dorfman have found that the individual variability in the excretion levels of these hormones is to some extent correlated with the physical development of the subjects.

With several hormones being produced and interacting on each other, the variations in the timing, character and magnitude of adolescent growth and sexual differentiation are readily understandable. Furthermore, with the production of both male and female sex hormones by both sexes, and in different amounts between individuals, various degrees of femininity in boys and masculinity in girls are to be expected. In considering many of the variables in both sexes, as, for example, late development in girls with broad shoulders, narrow hips and considerable body hair as contrasted with early development in boys with broad hips, narrow shoulders and sparse body hair, differences in the balance of the sex hormones from the usual occurrence may be assumed. Nathanson and Aub cite an example of striking change from obvious feminine identification in 2 boys toward masculinity associated with a rise in the androgen-estrogen ratio from estrogen excess to androgen preponderance. Further studies are required to demonstrate the relations between individual variability in hormonal excretions and growth and maturation.

#### FACTORS CONTRIBUTING TO GROUP DIFFERENCES IN GROWTH AND DEVELOPMENT OF NORMAL ADOLESCENTS

A better understanding of the normal physical and physiologic changes of adolescence, and particularly of the variability in their manifestations, which is consistent with good health and satisfactory ultimate development, would undoubtedly lead to more rational management of many of the so-called "problems of adolescence." It is not suggested that these problems do not require attention, but rather that the recognition that they are in many cases essentially physiologic would result in more conservative therapy and in greater emphasis on hygienic living. Frank<sup>71</sup> has called attention to some of the implications of what is known about growth and development during the adolescent years in respect to the policy and program of care for adolescent from a health standpoint. Shorr<sup>72</sup> approaches such endocrine problems from this point of view and has discussed the management of the usual ones. He takes the position that most of these can best be handled by a sane program of physical and mental hygiene, planned from the point of view that they are in the main expressions of physiologic variations.

It is now fully established that hormones elaborated by the endocrine glands are primarily responsible for the events that have been shown to occur in connection with the progress of a child toward maturity. Nevertheless, it is of interest to consider what conditions may lead to variations in hormonal activities and hence to differences between individuals or groups during this period. Since this report is concerned with normal occurrences, the effects of congenital abnormalities, defects, accident and disease will not be considered.

Racial and familial traits have long been recognized as important predeterminers of group as well as of individual characteristics. The extensive literature bearing on these hereditary factors cannot be reviewed here, but it is clear that any effect brought about by environmental factors can operate only within the limitations imposed by the genetically determined qualities and potentialities of the initial germ plasm. Boas<sup>73</sup> devotes much attention to the parts played by heredity and environment in bringing about family and racial differences. He has found that certain traits, such as the form of the head and face, are much more strongly influenced by race or family pattern than are others like height and weight. From statistical analyses of extensive studies, however, he concludes that even facial characteristics are modified by changes in environment. Hence, it is unwise to assume that any physical attribute is entirely determined by heredity or cannot be modified by environment. In clinical practice it is important to recognize individual characteristics that are constitutional in character and that may impose physical limitations or lead to ex-

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

## CASE 32221

### PRESENTATION OF CASE

A fifty-three-year-old Navy veteran entered the hospital because of dysphagia.

The patient was apparently well until three years before admission, when his ship was torpedoed. Hereafter he became quite "nervous." Four months before entry, he noted during luncheon the sudden onset of inability to swallow. He continued to have similar attacks several times a month, but they occurred only during periods of nervous excitement. During an attack a piece of solid food would "get caught in the neck", it was usually vomited immediately, but occasionally it was swallowed. Once the first solid food had passed, the remainder of the meal followed fairly readily. He had little trouble with liquid or soft foods. One month before entry, the patient vomited some bloody material while waiting in the Out Patient Department. He was immediately admitted to the Massachusetts Eye and Ear Infirmary, where a barium swallow showed a questionable lesion of the lower end of the esophagus. A chest film was normal. An esophagoscopy showed injection of the mucosa and engorged vessels near the cardia, and the operator gained the impression that a hard mass was pushing the esophagus forward, thus narrowing the lumen, no ulceration was seen. A biopsy specimen from this region showed slight chronic inflammation and edema. Examination of the blood showed a red-cell count of 2,530,000, with 8.6 gm of hemoglobin, and a white-cell count of 5800, with 57 per cent neutrophils. He was then discharged to the Out Patient Department.

He did well at home, eating everything, including hard biscuits, and gaining a few pounds in weight. Two weeks before entry he was again seen at the Eye and Ear Infirmary for a repeat esophagoscopy. The findings were identical with the previous ones. A No 22 bougie passed the lower third of the esophagus with difficulty. The biopsy specimen showed acanthosis, slight chronic inflammation and edema. A barium swallow was reported as indicating some esophageal obstruction. A gastro-

intestinal series revealed a constantly deformed duodenal cap, but no ulcer crater was demonstrated. Examination of the blood showed a red-cell count of 3,720,000, with 10.5 gm of hemoglobin, and a white-cell count of 6600.

Two days before entry, the patient was unable to swallow even milk "because of nervousness." Afterward he was able to eat a full meal. The patient stated that he lost 20 to 30 pounds in weight during the four months before admission. He gave no history of epigastric distress, intolerance to fatty foods, jaundice or melena.

Physical examination revealed a somewhat emaciated man who was in no acute distress. The heart was normal. A few crackling rales were heard at the bases of the lungs. The abdomen and extremities were negative.

The temperature, pulse, and respirations were normal. The blood pressure was 130 systolic, 78 diastolic.

Examination of the blood revealed a red-cell count of 4,000,000, with 70 per cent hemoglobin, and a white-cell count of 7900 with 57 per cent neutrophils. The total proteins were 6.3 gm per 100 cc, and the chloride 104 milliequiv per liter. The urine was normal. The stools were brown, and one of two specimens gave a positive guaiac test.

X-ray examination of the chest showed no abnormality. Another gastrointestinal series revealed no difficulty in the act of swallowing. The esophagus showed some tubulation of the lower 2 or 3 cm and an apparent soft-tissue thickening just about the cardia. Small soft-tissue masses seemed to project into the gas bubble, and barium was seen to "squirt" from the cardia across the gas bubble. Fluoroscopically the stomach appeared normal, with the exception of considerable thickening of the gastric rugae. On the film, however, there was questionable rigidity on the cardiac side of the fundus. The duodenal cap was again constantly irregular and deformed, it also showed an irregular fleck in the center of the cap measuring about 0.5 cm in diameter. The upper small intestine was not remarkable.

Two additional esophagoscopy biopsies showed acute and chronic inflammation. On the fifteenth hospital day an operation was performed.

### DIFFERENTIAL DIAGNOSIS

DR EARLE M CHAPMAN: May we see the x-ray films?

DR JAMES R LINGLEY: These films of the lower esophagus show the rigidity and irregularity that was referred to in the summary and, in addition, a suggestion of a mass above the cardia pressing on the gas bubble of the fundus. The same thing is seen in this film, a soft-tissue mass projecting into the fundus of the stomach. In this view, taken in the upright position, the barium seems to swerve across the base instead of passing along the lesser curvature.

study, but they are doubtless related to differences in the incidence of illnesses in early life, to dietary habits, to habits of activity and to other more obscure factors generally referred to as socio-economic

The physician dealing with a child who is under-size or otherwise underdeveloped cannot determine to what extent these features are due to heredity and to what extent to faulty diet or hygiene or to disease. If one or both of the child's parents show similar characteristics, the physician may be tempted to accept a genetic explanation as fully satisfactory without appreciating that in all probability environmental factors have played some part and possibly a dominant one. His assumption in itself tends to block further study and to keep him from devoting attention to diet and hygiene. It appears to be a more rational approach, and certainly one more in accord with recent findings, to assume that both hereditary and environmental factors are operative to some extent in all cases. Hence, heredity should never be accepted as the sole or even the principal factor in a given case until a thorough investigation has failed to reveal other retarding influences, or until correction of faulty environmental influences has been accomplished to the fullest possible extent.

Medical supervision of the care of infants and young children has unquestionably contributed greatly toward better health and development during these early years. This has been made possible by intensive study of the normal course of events as well as of the special problems at these ages. Medical supervision during the adolescent years can undoubtedly contribute much toward better health and more generally satisfactory development during this period also, and hence toward a higher standard of physical fitness at maturity. This progress, however, is dependent on further research and a better understanding of the normal course of events and the special problems of these years.

55 Shattuck Street

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specimens, and both of them were negative, but I ought from the whole picture that the patient had carcinoma of the cardiac orifice and that he should be explored by the transthoracic route, with a cooperative diagnosis of carcinoma

DR. LINGLEY I also disagree with Dr Chapman wonder what type of benign tumor can involve the esophagus and the stomach By x-ray there is definite involvement of the esophagus

DR. CHAPMAN I got the impression in reading the description that a mass was pushing the esophagus aside

DR. LINGLEY That was by esophagoscopy

DR. CLAUDE E. WELCH Two or three of our resected stomachs every year show evidence of duodenal ulcer when the primary lesion is a cancer of the stomach

#### CLINICAL DIAGNOSIS

Carcinoma of the stomach

#### DR. CHAPMAN'S DIAGNOSES

Cardiospasm

Polypoid adenoma of stomach.

Gastritis

Duodenal ulcer

#### ANATOMICAL DIAGNOSIS

Carcinoma of cardia of stomach, with periesophageal extension

#### PATHOLOGICAL DISCUSSION

DR. MALLORY This patient was explored by the transthoracic route A gastrectomy was performed, the resected specimen including the lower portion of the esophagus A scirrhus carcinoma of the cardia was found This had invaded upward in the outer wall of the esophagus, narrowing it from external pressure without growing out into the mucosa of the esophagus at any point So it is natural that Dr Benedict's biopsy specimens did not show tumor They had not gone deep enough, and should not have gone deep enough, to reach this tumor in the outer layers of the esophageal wall

DR. CHAPMAN Is that not a rare location for a scirrhus type of carcinoma?

DR. MALLORY They are much less frequent in that area than in other parts of the stomach

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#### CASE 32222

#### PRESENTATION OF CASE

*First admission* A fifty-five-year-old liquor dealer entered the hospital because of weakness and tarry stools

The patient was in apparent good health until one year before entry, when he had an episode of pain and weakness in the left lower quadrant of the abdomen X-ray films taken at that time showed no abnormality He recovered completely Five months before entry, on his return home after a hard day in his store, he suddenly felt "sick at his stomach" and fainted following urination Afterward he felt very weak and passed some tarry stools A local doctor called the next day and found a marked anemia Another gastrointestinal series was negative The patient gradually regained full strength but continued to pass occasional tarry stools Ten days before entry the patient had another episode of weakness followed by tarry stools mixed with gross blood The patient had suffered from gout for many years

Physical examination revealed a well developed man in no acute distress showing marked pallor of the skin and mucous membranes The lungs were clear A soft systolic murmur was heard at the apex There was some tenderness to deep palpation in the left lower quadrant Proctoscopic examination was negative

The temperature, pulse and respirations were normal The blood pressure was 120 systolic, 80 diastolic

The examination of the urine was negative The blood showed a red-cell count of 2,150,000, with a hemoglobin of 6.6 gm and a hematocrit of 20 The white-cell count was 6400, with a normal differential The nonprotein nitrogen was 40 mg per 100 cc, the serum protein 6.5 gm, and the uric acid 6.6 mg The prothrombin time was 21 seconds (normal, 18 to 20 seconds), the bleeding time 2.5 minutes, and the clotting time 10 minutes The blood Hinton reaction was negative A stool specimen gave a negative guaiac test A gastrointestinal series with hourly films showed the esophagus, stomach and small bowel to be normal A barium enema was also negative

The patient was given three blood transfusions of 500 cc each On the tenth hospital day an exploratory laparotomy and appendectomy were performed No cause of the gastrointestinal bleeding could be found He recovered uneventfully and was discharged on the nineteenth hospital day

*Second admission* (two months later). Despite the occasional passage of occult blood in the stools, the patient felt well until six days before his second admission, when he returned from a two-day hunting trip feeling "all in" After the evening meal he became nauseated but had no pain The nausea and weakness persisted until the day of admission, when the local doctor found the blood pressure to be 80 systolic, with the diastolic pressure unobtainable An enema on the previous day was said to have produced a grossly bloody stool He had not vomited at any time during his illness

as it normally does. The film of the chest shows a normal heart and lungs, but it suggests a mass in the region demonstrated in the gastrointestinal film. I think that the observation of an ulcer crater in the duodenum must have been that of the fluoroscopist. The films show deformity but no definite crater that I can make out.

DR CHAPMAN: It seems obvious to me that we are dealing here with evidence of a tumor of the stomach, and so it comes down to a question of type. Was it a benign tumor or a malignant tumor? If we paraphrase the history, briefly, we have a man of fifty-three who suddenly had difficulty in swallowing, vomited blood, had an anemia, had lost a good deal of weight, had guaiac-positive stools and had a mass in the fundus of the stomach, it is a temptation to make a diagnosis of malignant tumor, which would be a sound clinical diagnosis.

On analysis of some of the clinical features in this case, however, I rather favor the possibility that this lesion was some benign condition. So we have to think of the benign lesions that can produce this syndrome in a man of fifty-three. To begin with, we have the fact that he had been nervous and emotionally upset. He then had what sounds like a typical description of cardiospasm, because although at times he could swallow solids and fluids, at other times, after being emotionally upset, he could not even swallow liquids. Another strong clinical point is the absence of pain. Carcinoma usually produces pain, but we do know that about 10 per cent of such patients may be without pain, and in Osler's<sup>1</sup> original series of 160 patients with extensive carcinoma of the stomach, 20 had no pain. Another clinical point is the improvement in the anemia, which is unexplained. When the patient first came in he had a red-cell count of 2,500,000, but later, just before operation and I judge without transfusion, the count was 4,000,000, with a hemoglobin of 70 per cent. That is another point against a malignant lesion. The third clinical point against a malignant lesion is that the rugae were thickened and that a duodenal ulcer was present, a combination that is most unusual in a person with carcinoma higher up. The association of duodenal ulcer and cancer of the stomach is quite rare.

If it was a malignant lesion, what type could it be? In this region it should be the medullary type, a large cauliflower-like growth that invades all layers of the stomach and produces villous-like projections into the stomach. It can produce the picture that Dr Lingley has described, but this man was operated on and apparently did not come to autopsy, and I have a hunch that he is still alive. If it was a medullary carcinoma, he might have had metastases in the lungs, and yet there is no evidence of metastases in the chest films.

If it was a benign lesion, what type could it be? There are several types of benign tumors of the stomach. One is a bezoar, sometimes found in

nervous people. I cannot believe that a bezoar would do this, nor can I believe that this was one of the rare types of tumor, such as myxoma, fibroma, or a cystic tumor. One tumor that falls midway between the extremely malignant and benign forms is lymphoma. It is too bad that we do not have a complete blood picture, although I do not believe that a differential count would have substantiated a diagnosis of lymphoma.

There is one other type of benign tumor that this might be, that is, a so-called "polypoid adenoma," which is seen in older people in the presence of gastritis. In Winternitz's<sup>2</sup> case there were multiple tumors not only in the stomach but throughout the intestine, and also multiple skin tumors of the hemangioendothelioma type. I looked carefully to see whether skin tumors were described on physical examination, but none were reported.

The biopsy diagnosis of acanthosis is a puzzling point.

DR MALLORY: Leukoplakia might have been a better word to use — and a more familiar term.

DR CHAPMAN: The word acanthosis made me think of a rare skin condition known as acanthosis nigricans, which is often associated with cancer of the stomach, but the clinical record gives no indication of skin pigmentation, so that acanthosis nigricans is unlikely.

Finally, because of these four clinical points — the absence of pain, the improvement in the anemia, the presence of a duodenal ulcer and the existence of cardiospasm without proof of carcinoma from four esophagoscopies — I am going to say that this patient had a polypoid adenoma of the stomach.

I have one other comment to make. Here is another case in which the endoscopist and the roentgenologist have not been able to make a positive diagnosis. I think that that is chiefly because of the mechanical difficulties consequent to the location high in the fundus, where examination is difficult.

DR TRACY B. MALLORY: Dr Benedict, you esophagoscoped this patient. Let us hear your views.

DR. BENEDICT: I do not agree with Dr. Chapman in two respects. First, he says that cancer of the stomach is usually a painful process. There is no pain whatever in many cases of cancer of the stomach. Second, I think that the x-ray interpretation was of great help in this case. Dr. Lingley has just described a rigid terminal portion of the esophagus, with, I think he said, a mass infiltrating the fundus of the stomach. To my mind, that is fairly typical of carcinoma arising in the stomach and infiltrating the lower esophagus. I had made up my mind to that before Dr. Mallory showed me the record.

I did an esophagoscopy on this man twice, and both times I met complete obstruction at the cardiac orifice. I then tried to pass the gastroscope, but it also met complete obstruction. When the gastroscope meets complete obstruction at the cardiac orifice it usually means cancer. I did get biopsy



This also does not rule out gastritis because we do not know when the gastroscopy was performed — how long after the hemorrhage, which he had seven days after admission. Gastritis may heal rapidly and not be demonstrable after a bleeding episode. I do not believe, however, that gastritis is the diagnosis because it is unlikely without any other symptoms and a negative gastroscopy.

We might consider such a rare condition as telangiectasia, a hereditary condition, which does occur in the stomach, but since it is associated with cutaneous and mouth lesions, which this patient did not have, I think that it can be discarded.

We come now to the hiatus hernia. A hiatus hernia may bleed, but it is generally a slow oozing. Massive bleeding does rarely occur and is usually associated with gastritis or ulceration in the mucosa of the hernia. Since there was no evidence of that by gastroscopy or esophagoscopy and since he had no other symptoms, I do not believe that that was the cause of the bleeding.

Did he have a tumor of the small intestine, which might easily have been missed by x-ray examination, such as a leiomyoma, an adenoma or a neurogenic tumor? That is a possibility but I doubt that it was the cause.

Could he have had a tumor of the stomach that was missed by all these examinations? If he had a small carcinoma, it would be extremely unlikely that he had no other symptoms except bleeding. Massive hemorrhage from carcinoma is quite unusual, particularly in a person who has had repeated hemorrhages over a long period of time.

Did he have a benign tumor of the stomach, such as a polyp or leiomyoma? Either of these tumors may be small and may ulcerate and bleed, particularly a leiomyoma, and may be missed by x-ray examination.

In view of such completely negative findings I can do no more than guess, but I shall suggest a diagnosis that is most consistent with the symptomatology given, even though it is a rare condition. I think that the symptomatology of the patient fits in best with a leiomyoma of the stomach. This tumor is often associated with repeated massive hemorrhages without any other symptoms. It must have been a small one to have been missed by x-ray examination and exploration, but for the reasons given the other usual causes of bleeding are unlikely.

DR. TRACY B. MALLORY: Dr. Benedict, have you any comment?

DR. EDWARD B. BENEDICT: I thought that on a statistical basis this was fairly likely to be a duodenal ulcer in spite of the negative examination and the negative exploratory laparotomy. Even if one sees the stomach and duodenum at operation one cannot always see the lesion. I believed that he should have a resection on the basis that he was bleeding from the duodenum.

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Gastrointestinal hemorrhage (ulcer?)

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Leiomyoma of stomach  
Gout

## ANATOMICAL DIAGNOSES

Gastric ulcer, acute  
Gastritis, acute

## PATHOLOGICAL DISCUSSION

DR. ARTHUR W. ALLEN: I explored this man two or three months before his ultimate operation. At that time I went over his entire gastrointestinal tract as carefully as I could, having in mind particularly that this might have been a small-bowel lesion. Early tumors of the small intestines are extremely difficult to pick up in the x-ray examination, even with the so-called "small-bowel enema." The exploration was absolutely negative. My own reaction about it was that if he had had a duodenal ulcer that had caused three bouts of hemorrhage we should have found some indication of scarring, even if we could not feel a crater. Since the duodenum never looks normal after there has been an ulcer that has bled massively, one always has some lead that the disease is in that region. But this duodenum was absolutely normal. There was nothing abnormal that I could palpate throughout the length of the small bowel. I was not so happy about palpation of the colon because the large bowel was not completely empty at the time of exploration. But even when the colon is empty, it is sometimes difficult to palpate a polyp. On the other hand, satisfactory barium enemas had been performed, and the roentgenologists can diagnose polyps by that method quite accurately. So I did nothing except the exploration and appendectomy, being still in doubt about the source of his bleeding.

We have a certain number of patients who bleed massively from the gastrointestinal tract in whom we cannot find the cause or source of hemorrhage. Of course the majority of them have a definite lesion that can be so demonstrated by our various examinations that we are quite sure of the diagnosis. Then there is a small group that have lesions that we suspect as being the source of bleeding, the chief one of these being diverticulosis, although we are never quite certain about that.

The reason that this man was operated on the second time is that we thought he was going to bleed to death if we did not do something about it. We had information for the first time after gastroscopy, which caused him to have blood in the vomitus, indicating that the source of the bleeding was high. Based on the experience of just one other case that we had here a few years ago, in which all examinations except that for gastritis

Physical examination revealed a pale, anemic and weak-appearing man with no acute complaints. There was minimal deep tenderness over the cecal region. Proctoscopy was again negative.

The temperature, pulse and respirations were negative. The blood pressure was 102 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 5.5 gm. The white-cell count was 5000, with 73 per cent neutrophils. The urine was negative. Three stool specimens gave strongly positive guaiac tests.

A gastrointestinal series and a barium enema were entirely negative except for a hiatus hernia of the stomach measuring 2.5 cm in diameter. On the morning of the seventh hospital day the patient vomited four times following the administration of 0.5 mg of colchicine. The vomitus had the appearance of coffee grounds.

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Do you care to show the x-ray films, Dr. Lingley?

**DR. JAMES R. LINGLEY:** They are negative.

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**DR. LINGLEY:** That is correct, the films do not add anything.

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The physical and laboratory examinations reveal nothing other than signs of marked anemia and an elevated uric acid, which would be expected with gout. I do not know how to evaluate the pain in the left lower quadrant or the tenderness in this region noted at the first admission, but in view of the negative barium enema, negative proctoscopy

and negative laparotomy I am inclined to discount it as unimportant. One thinks of diverticulitis, but such a lesion does not bleed.

There is nothing to suggest that a primary blood disorder caused the hemorrhages. We can dismiss gout as playing a role in the picture except to comment on the fact that he probably had an acute attack, although the record does not state it, at the time of the second admission because he was given colchicine. This resulted in, or rather was followed by, vomiting of coffee-grounds material. One tablet of colchicine is unlikely to produce vomiting. Acute attacks of gout occur typically in a gouty person following such upsetting episodes as an operation, a trip, a hemorrhage and an infection. So I am not surprised that he had attacks after these hemorrhages.

The first problem is to try to place the location of the hemorrhages. The stools were described as tarry on several occasions but gross blood was noted on two occasions. Blood from the colon may be dark but is rarely dark enough to be termed "tarry." Tarry stools usually mean that the bleeding is coming from the stomach or small intestine. The fact that he had grossly bloody stools also does not necessarily suggest a large-bowel lesion, since bright red blood may appear in the stools after a hemorrhage from the stomach provided intestinal motility is fast enough. He only vomited once, and the vomitus was described as coffee-grounds in appearance, which is strong evidence that the blood came from the stomach or duodenum. The possibility of multiple lesions arises. Polyposis, both of the colon and stomach, is a rare entity. In the presence of negative proctoscopic, gastroscopic and x-ray examinations it may be excluded. All in all, the evidence points to the bleeding from the stomach or small intestine.

Could this have been due to an extragastric cause, such as cirrhosis or Banti's disease? The patient was a liquor dealer, but that does not mean that he drank excessively or at all. The two recorded white-cell counts show a slight leukopenia, but in the absence of esophageal varices, which ought to be demonstrable by x-ray examination or esophagoscopy, and of splenomegaly and in the presence of a negative laparotomy I think that we can exclude cirrhosis and Banti's disease.

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## GAMMA GLOBULIN IN ACUTE HEPATITIS

IN THE October 4, 1945, issue of the *Journal*, the Massachusetts Department of Public Health announced the initiation of a program for the provision of blood and blood derivatives without cost to the citizens of Massachusetts. Among the blood derivatives that it hopes to provide is gamma globulin, which is prepared in such a manner as to contain in a concentrated form most of the antibodies that are normally found in human plasma. A number of studies by workers in different localities have been made in collaboration with Dr Edwin J Cohn and his associates in attempts to determine the prophylactic and curative value of gamma globulin in various infections. The results of several

such studies with respect to infectious hepatitis, formerly called "catarrhal jaundice," have already become available.

Stokes and Neefe<sup>1</sup> tested the prophylactic value of intramuscular injections of gamma globulin during an epidemic of infectious hepatitis in a summer camp for boys and girls. There were 331 children who had had no signs of disease when they began their study, and 53 of these were injected with gamma globulin, using an arbitrary dose of 0.15 cc per pound of body weight. Among those who received these injections, only 3 developed jaundice, but 8 additional children developed symptoms and laboratory evidence of hepatitis without overt jaundice. The icterus in the 3 cases was visible only in the scleras and not in the skin. Of the 278 children who did not receive globulin injections, 125 developed jaundice and 60 had evidence of hepatitis without jaundice. Thus, the total incidence of infection among the globulin recipients was 21 per cent, as compared with 67 per cent among the controls, a difference that is statistically significant. The average duration of icterus was about five days in the injected cases, and more than fourteen days in the control cases. Furthermore, the onset of hepatitis in the 11 patients who received gamma globulin occurred in every case during the first ten days following injection, whereas cases continued to appear among the controls for thirty-two days.

On the basis of this report, field studies on the prevention of hepatitis were conducted during an outbreak of this disease in a bombardment group based in the Mediterranean Theater of Operations during the fall and winter of 1944-1945.<sup>2</sup> The dose of gamma globulin chosen for this study was 10 cc, which was found to be the largest amount that could be injected without affecting the full-duty status of the men. Globulin was given to members of two squadrons and to a headquarters group, whereas those belonging to two other squadrons served as controls. Each of the squadrons had about 500 men, and all were quartered on the same field. Among the injected squadrons there occurred 3 cases of hepatitis with jaundice. Two of these cases occurred in persons who, for some reason or other, had not received the globulin injections. The third developed jaundice only of the scleras, and this began

were negative, we decided on subtotal gastrectomy. The first man, who was about the same age as the one under discussion today, had repeated hemorrhages and came back every three or four months exsanguinated. We finally did a subtotal gastrectomy on the basis of gastritis and found a lesion that was similar to the one discovered in today's case, which Dr. Mallory will describe.

DR. CLAUDE E. WELCH: The second operation was done after the decision had been made that we could not stand idly by, it was a matter of getting the patient into shape and doing, let us say, a blind subtotal gastric resection. The only important findings at operation were a few adhesions in the lesser omental sac, just behind the pylorus. Everything else was so negative that I thought Dr. Castleman should come to the operating room himself to be sure that we did not make any holes in the specimen.

DR. MALLORY: Dr. Castleman, will you tell us what you found?

DR. BENJAMIN CASTLEMAN: In the central portion of the stomach there was a small but definite superficial ulceration surrounded by a smaller and even more superficial erosion. There was no evidence at that time that the patient was still bleeding. As soon as I told Dr. Welch that I had found something he was delighted. He was afraid that the stomach would prove to be normal. The fact that we did find an erosion and a superficial ulceration satisfied him.

DR. MALLORY: The sections from the stomach showed a moderately severe gastritis well down in the pyloric area, where Dr. Benedict might not have been able to see it. In this area there was a very shallow erosion. One could just barely call it an ulcer, still it was quite active, with beginning healing at the margins. It is reasonable to say that that was the cause of the hemorrhage.

among battle casualties who had received transfusions of blood or plasma. Reference is also made to an experimental study that indicated that one preparation of gamma globulin had no neutralizing antibodies for one causative agent of serum hepatitis. The exact basis for the discrepancies has not yet been clarified. Thus, the prophylactic value of gamma globulin in the prevention of homologous serum jaundice remains uncertain.

Gamma globulin apparently has a definite place in the prophylaxis of infectious or epidemic hepatitis, that is, so-called "catarrhal jaundice." It is hoped that the Massachusetts program will receive enthusiastic support so that provision of gamma globulin for that purpose and for its use in other conditions in which it has proved effective will be possible. It should be borne in mind, however, that gamma globulin is not effective in modifying infectious hepatitis if given after symptoms have appeared and that at the present time its effectiveness in the prevention of homologous serum jaundice is not definitely proved.

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MOTORCADE

THE most contumacious lover of living horseflesh must admit, after the passage of these fifty-odd years, that the automobile has come to stay. As the horse was to the cowboy, the circuit rider and the doctor of yesterday, so is the automobile today to the doctor, the salesman, the baker and the candlestick maker, multiplied a million times. The automobile is here in our outmoded town and city streets, we cannot ignore it, we cannot make it disappear by banning its parking or, if it is parked, by plastering it with tickets. It is to these millions a vital part of their bread-winning capacity, the very officer who makes the

stream of traffic halt at his command, succeeding where King Canute failed, or who occupies his time chalking the tires of potential overtime parkers, mounts his own chariot, his duty done, and drives away like Jehu the son of Jehoshaphat, or Mr Toad of Toad Hall. His hunting over he joins the exodus, immune, perhaps, from becoming one of the hunted.

It cannot be doubted that many of our citizens, commonly respected and accepted as decent members of society, legally married and the parents of small children, still have two sides to their characters — the Dr. Jekyll side, using their reputations as a sort of guarantee of irreproachable conduct, and the Mr. Hyde side, the latter manifesting itself when they are behind the wheels of moving automobiles. There is a hypnosis to swift vehicular travel that affects us all somewhat as it did the reptilian hero of *The Wind in the Willows*. It sets us on edge, it removes our sense of propriety and puts us in open conflict with all our fellows, even if it does not turn us into the scoundrels that the law, afoot or awheel, seems to consider all human beings awheel to be. All scoundrels, it is true, may at times drive motor cars, it does not follow that all drivers of motor vehicles are to be considered scoundrels until proved otherwise.

The physician, parenthetically, setting himself aside from other individuals and classes of men, although not above them, feels that there is a particular urgency about his use of the automobile, that to serve the public best he should be in a position to travel in his car with reasonable dispatch to minister to his patients, to visit his hospital or to reach his office, and to leave his car in legal, if not in physical, safety when he has arrived at any of these destinations.

Up to the present time the efforts of our traffic authorities, although zealous, appear to the conscientious driver to have been at times somewhat shortsighted. They have been designed primarily to speed up traffic flow with only secondary thought being given to the terminals and way stations at which that traffic must stop. Insufficient consideration is given to the facts that every driver is theoretically on some legitimate errand — the term "pleasure car" being now an outdated misnomer — and that to discharge his mission he must bring his

9 days after the injection. In the same period, 25 cases of hepatitis with jaundice occurred in the control squadrons. Previous to the time of the globulin injections, there had been 95 cases in the injected groups and 116 cases in the control groups.

A second study was undertaken in three groups of ground forces among which an epidemic of hepatitis had already started. Injections of 10 cc of gamma globulin were given to varying proportions of the strengths of these three groups — 40 per cent of one, 10 per cent of another and 25 per cent of the third. The groups consisted of 1089, 9101 and 1868 men, and they were followed for twelve, seven and five weeks, respectively, after the injections. A total of 9 cases of jaundice developed in the injected persons, an incidence of 0.5 per cent, as compared with 335 cases, or an incidence of 3.3 per cent, among the controls.

Havens and Paul<sup>3</sup> also conducted a study on the prevention of infectious hepatitis during an epidemic in a Catholic home for children in New Haven, Connecticut. Doses ranging from 5 to 10 cc of gamma globulin were used, depending on the weight, the average being 0.08 cc per pound. Gamma globulin was given to 97 children, whereas 155 served as controls. Jaundice occurred in 2 of the inoculated children, and in 36 of the controls. There were 6 additional cases of hepatitis without jaundice in the protected group, and 17 among the controls. Thus, 8 per cent of the inoculated group came down with the disease, as compared with 34 per cent of the controls, and the incidence of cases of overt jaundice was more than ten times as frequent among the latter.

All these results indicate quite definitely that gamma globulin given to susceptible persons after exposure to or during the incubation period of infectious (epidemic) hepatitis usually prevents the disease, and that the disease is attenuated in most of those who become infected after inoculation. The passive immunity seems to last at least six or eight weeks.

Studies with gamma globulin in measles had suggested that it was of value in lessening the severity and in shortening the course of that disease if given soon after the onset of symptoms. In view of the long illness and convalescence in cases of infectious

hepatitis, it seemed worth while to determine whether gamma globulin had a similar attenuating effect in this disease. A study of this aspect was made during an outbreak of infectious hepatitis in the air forces in the Mediterranean Theater of Operations.<sup>4</sup> Two hundred and seventy-eight patients admitted to the hospital with a tentative diagnosis of infectious hepatitis were studied. Gamma globulin was given intramuscularly in doses of 0.3 cc per pound of body weight to alternate patients. No significant difference in the severity or duration of jaundice or in the duration of the positive methylene blue test in the urine was observed in the two groups of cases. This study suggests that there is no attenuating effect of gamma globulin when given in these doses early in the course of infectious hepatitis.

Additional studies have been undertaken to determine whether gamma globulin also serves to prevent so-called "homologous serum jaundice." One such study was undertaken in a large general Army hospital in continental United States after 100 cases of jaundice had been observed among battle casualties who had received transfusions of whole blood or plasma.<sup>5</sup> Casualties who had been wounded for less than four months and had received injections of various blood products but had not developed symptoms of hepatitis were chosen for this study. Alternate cases were given 10 cc of globulin on admission to the hospital, and this was repeated after one month. There were 384 cases in each group, and hepatitis with jaundice developed in 2.9 per cent of the globulin recipients, as compared with 11.5 per cent of the controls. In more than half the cases that occurred in the globulin recipients, the onset of symptoms of hepatitis occurred less than a week after globulin had been given. By contrast, more than three quarters of the cases that occurred among the controls began more than one week after admission. The results of this study suggest that the early administration of serum globulin was effective in preventing hepatitis in these cases. In an addendum to this report, however, mention is made of a similar study conducted at another large general Army hospital. In that study a single injection of globulin was used, and it seemed to have no effect on the incidence of homologous serum jaundice.



among battle casualties who had received transfusions of blood or plasma. Reference is also made to an experimental study that indicated that one preparation of gamma globulin had no neutralizing antibodies for one causative agent of serum hepatitis. The exact basis for the discrepancies has not yet been clarified. Thus, the prophylactic value of gamma globulin in the prevention of homologous serum jaundice remains uncertain.

Gamma globulin apparently has a definite place in the prophylaxis of infectious or epidemic hepatitis, that is, so-called "catarrhal jaundice." It is hoped that the Massachusetts program will receive enthusiastic support so that provision of gamma globulin for that purpose and for its use in other conditions in which it has proved effective will be possible. It should be borne in mind, however, that gamma globulin is not effective in modifying infectious hepatitis if given after symptoms have appeared and that at the present time its effectiveness in the prevention of homologous serum jaundice is not definitely proved.

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#### MOTORCADE

THE most contumacious lover of living horseflesh must admit, after the passage of these fifty-odd years, that the automobile has come to stay. As the horse was to the cowboy, the circuit rider and the doctor of yesterday, so is the automobile today to the doctor, the salesman, the baker and the candlestick maker, multiplied a million times. The automobile is here in our outmoded town and city streets, we cannot ignore it, we cannot make it disappear by banning its parking or, if it is parked, by plastering it with tickets.

It is to these millions a vital part of their bread-winning capacity, the very officer who makes the

stream of traffic halt at his command, succeeding where King Canute failed, or who occupies his time chalking the tires of potential overtime parkers, mounts his own chariot, his duty done, and drives away like Jehu the son of Jehoshaphat, or Mr. Toad of Toad Hall. His hunting over he joins the exodus, immune, perhaps, from becoming one of the hunted.

It cannot be doubted that many of our citizens, commonly respected and accepted as decent members of society, legally married and the parents of small children, still have two sides to their characters — the Dr. Jekyll side, using their reputations as a sort of guarantee of irreproachable conduct, and the Mr. Hyde side, the latter manifesting itself when they are behind the wheels of moving automobiles. There is a hypnosis to swift vehicular travel that affects us all somewhat as it did the reptilian hero of *The Wind in the Willows*. It sets us on edge, it removes our sense of propriety and puts us in open conflict with all our fellows, even if it does not turn us into the scoundrels that the law, afoot or awheel, seems to consider all human beings awheel to be. All scoundrels, it is true, may at times drive motor cars, it does not follow that all drivers of motor vehicles are to be considered scoundrels until proved otherwise.

The physician, parenthetically, setting himself aside from other individuals and classes of men, although not above them, feels that there is a particular urgency about his use of the automobile, that to serve the public best he should be in a position to travel in his car with reasonable dispatch to minister to his patients, to visit his hospital or to reach his office, and to leave his car in legal, if not in physical, safety when he has arrived at any of these destinations.

Up to the present time the efforts of our traffic authorities, although zealous, appear to the conscientious driver to have been at times somewhat shortsighted. They have been designed primarily to speed up traffic flow with only secondary thought being given to the terminals and way stations at which that traffic must stop. Insufficient consideration is given to the facts that every driver is theoretically on some legitimate errand — the term "pleasure car" being now an outdated misnomer — and that to discharge his mission he must bring his

space-occupying transport somewhere to a halt, and there leave it for a period of time

To solve urban traffic problems — and for Boston the proposed garage under the Common would be only a partial answer — convenient scattered terminals must be furnished in a suitable ratio to the volume of traffic. Levees along a river to confine and hasten the flow of water do not constitute effective flood control. What must be provided are extra basins into which the flood waters can be diverted and allowed to settle. Similar areas for automobiles are more important for what appears to be our immediate mechanical future than are wide sidewalks, grassy malls or extra traffic officers with even louder whistles and more pieces of chalk

## MASSACHUSETTS MEDICAL SOCIETY

### RESOLUTION CONCERNING REVIEW LECTURE COURSE

The following resolution was unanimously adopted by those physicians attending the last session of the Review Lecture Course on May 15

RESOLVED that we, the physicians who have attended the Review Lecture Course for former medical officers and practitioners, presented by the Massachusetts Medical Society and the Department of Public Health, Commonwealth of Massachusetts, do hereby express our thanks and deep appreciation to the officers of the Massachusetts Medical Society, the officials of the Massachusetts Department of Public Health, the members of the various committees concerned, the chairmen, the lecturers and all others who so ably participated in planning and carrying through to a most successful conclusion the excellent program that was made available to us

This program not only met the requirements of those recently returned from active service but also those of the busy practitioners who have been unable to attend many medical meetings during the war years

## DEATHS

ATWATER — James B. Atwater, M.D., of Westfield, died May 3. He was in his eighty-eighth year.

Dr. Atwater received his degree from the New York University Medical College in 1882. For thirty-seven years he was chief of staff at Noble Hospital, and since his retirement in 1934 chief-emeritus of that institution. He was a member of the American College of Surgeons, the American Academy of Medicine of New York, the New England Association of Railroad Surgeons and the Springfield Academy of Medicine, and a fellow of the American Medical Association.

Two sons, a sister, two grandsons and a granddaughter survive.

AYER — Thomas H. Ayer, M.D., of Westboro, died May 16. He was in his eighty-first year.

Dr. Ayer received his degree from the Bowdoin Medical School in 1893. He was a fellow of the American Medical Association. He retired in 1934.

EVANS — Miner H. A. Evans, M.D., of Wellesley Hills, died May 5. He was in his sixty-sixth year.

Dr. Evans received his degree from Harvard Medical School in 1902. He became assistant physician at the Danvers State Hospital and later became associated with the Adams Nervine Asylum. He established a private practice in Roxbury in 1906 and was also a member of the staffs of the neurologic services of the Boston Dispensary and the Carney Hospital. Later, he became associated with the Dorchester Free Dispensary, the Boston Psychopathic Hospital and the Boston City Hospital. At the time of his death, he was consulting physician in neurology and psychiatry at the Quincy City Hospital and visiting physician in neurology at the Boston City Hospital. He graduated in 1915 from the Boston University Law School and was later admitted to the Massachusetts and the United States bars, having been a consultant in many criminal trials. He was a member of the American Psychiatric Association, New England Society of Psychiatry and Neurology, Massachusetts Society of Psychiatry and Boston Society of Psychiatry and Neurology and a fellow of the American Medical Association.

His widow and two daughters survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Salem	June 3	Paul W. Hugenberger
Haverhill	June 5	William T. Green
Lowell	June 7	Albert H. Brewster
Greenfield	June 10	Charles L. Sturdevant
Gardner (Worcester Sub-clinic)	June 11	John W. O'Meara
Brockton	June 13	George W. Van Gorder
Pittsfield	June 17	Frank A. Slowick
Springfield	June 18	Garry deN. Hough, Jr.
Worcester	June 21	John W. O'Meara
Fall River	June 24	David S. Grice
Hyannis	June 25	Paul L. Norton

Physicians referring new patients to clinic should get in touch with the District Health Officer to make appointments.

## CORRESPONDENCE

### LOCAL INJECTION OF PENICILLIN

To the Editor: The following observations are offered in regard to the article "The Regional Injection of Penicillin in Local Infections," by Rose and Hurwitz in the February 28 issue of the *Journal*.

Injections of penicillin in saline are ordinarily painful. Given by the method described, in which the authors recommend "injecting slowly ahead of the needle, and progressing toward the center of infection," the injections may be severely painful, even if one avoids inserting the needle into the inflammatory area.

In my experience, this pain can be minimized by inserting the injection needle through a small skin wheal of 1 per cent procaine, thrusting the needle into the depth desired and then making the injection of penicillin as the needle is withdrawn. In our hands, this method has been effective in the treatment of large furuncles without incision. I have not added procaine to the penicillin solution itself. According to Hirsh and Dowling (*Am J M Sc* 210 435, 1945), however, small amounts of procaine would have no detrimental effect on the action of the penicillin.

JAMES G. TELFER  
Surgeon, U.S.P.H.S.

United States Marine Hospital  
Fourteenth Avenue and Park Boulevard  
San Francisco

(Notices on page xv)

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## HEALTH BILLS PENDING IN CONGRESS\*

### Part Four

FRANZ GOLDMANN, M.D.†

NEW HAVEN, CONNECTICUT

**JULIAN HUXLEY** once wrote, "To speculate without facts is to attempt to enter a house of which one has not the key." The desire to avoid speculation and obtain factual information on pending health legislation seems to be strong, judging from the fact that some of the bills are on the best-seller list of the Superintendent of Documents in Washington.

Important organizations, representing large groups of the population, have officially endorsed the major legislative proposals now in Congress. Many people from all walks of life favor government action in the whole field of health service, on the ground that protection of the right to health care is a fundamental function of any society aspiring to a genuine and rational economy of human resources and values.

#### ATTITUDE OF THE MEDICAL PROFESSION

In general, the medical profession supports the hospital survey and construction program embodied in the Hill-Burton Bill, the expansion and improvement of general public-health, maternal and child health services proposed in Title I of the National Health Bill, disability insurance as recommended in the Wagner-Murray-Dingell Bill of May, 1945, and federal aid for medical research and education as proposed in the National Science Foundation Bill, the Mental Health Bill, the National Health Bill and other pertinent measures.

But the physicians are not unanimous in their opinions on pending health legislation. A few insist that they are against any plan, and resent any encroachment on what they believe to be their own territory. Others prefer to pass responsibility to the economists by maintaining that if the standards of economic independence of the poor and the indigent are raised, the problem of medicine will take

care of itself. Still others doubt that any plan can be a success so long as certain evils are permitted to persist. A physician recently wrote to Senator Pepper, "As long as the United States is a place of easy divorce, quick-lunch counters and horn-tooting automobile drivers, and as long as the Smiths try to keep up with the Joneses, this will be a land of constipation, stomach ulcers, coronary thrombosis and emotional instability, and I don't think any 'plan' is going to help a great deal."<sup>1</sup>

Many are willing to accept government participation in the organization of medical care, provided that it is confined to service for the control of communicable diseases, care of the mentally sick and defective and programs for the needy and special groups, such as the veterans. Here and there voices of doubt can be heard questioning the wisdom of supporting the legislative proposals officially endorsed by organized medicine. Some writers point out that the Hill-Burton Bill leaves the door ajar for serious federal interference in local affairs. Some physicians fear that the Kilgore Bill would restrict the traditional freedom of scientific research by bringing politics into science.

What is of paramount significance is the unqualified opposition of the American Medical Association to compulsory health insurance, as proposed in the National Health Bill, and to a system of tax-supported medical care, as recommended in the Maternal and Child Welfare Bill. This attitude on the part of physicians is not universal. Two organizations of physicians, composed of members of the American Medical Association, have repeatedly gone on record in favor of compulsory health insurance. Early in 1946, the Committee on Medicine and the Changing Order of the New York Academy of Medicine stated its belief thus: "It may be desirable to conduct careful experiments at state and local levels with compulsory government insurance, so that we may have in the near future comparative experience with the relative values of voluntary and compulsory procedure."<sup>2</sup>

\*This is the last of a series of four lectures on medical sociology given at Harvard Medical School during February and March, 1946. They were sponsored by the Department of Preventive Medicine and were primarily intended for third-year students.

†Associate clinical professor of public health, Yale University School of Medicine.

Much of the opposition to legislative proposals dealing with medical care is due to misinformation concerning the contents of the bills, unfavorable personal experiences with some program, fear of a revolutionary change in the traditional pattern of practicing medicine and unfamiliarity of physicians with the history of organized care of the sick. As John Locke once wrote, "New opinions are always suspected and usually opposed, without any other reason but because they are not already common."

In the center of the debate at present is the method of compulsory health insurance. At the risk of laboring the obvious, it must be stated that health insurance by law is organized self-help financed by money that the self-supporting people are asked to save for the purpose of paying for their own care. What is changed by such legislation is the method of raising funds for the support of professional and institutional services. Instead of paying if and when service is received and in proportion to the amount of service rendered, people are required to pay in advance small average amounts, in return for which they are entitled to any or all of the services available under the program. What is not changed by such legislation is the institution of private practice of medicine, dentistry and related professions, the institution of voluntary hospitals and the institution of voluntary health agencies. Being, as it is, a method of organizing payment for medical care, compulsory health insurance is neither a cure-all for social evils nor the gateway to the millennium.

There is nothing new about compulsory health insurance. It was adopted in this country as early as 1798, when the Act for the Relief of Sick and Disabled Seamen was passed. At that time this method of raising money was considered the most equitable one, as Mr. Williamson stated in the House of Representatives. At present compulsory health-insurance programs are in operation in some thirty countries in Europe, Asia, South America and Australia, and in Mexico. The potentialities and limitations of this method are known to every student of the subject, and experience is more than ample. If Congress should pass the pertinent measure, it would be possible to avoid, rather than to repeat, the many mistakes made in sixty years of trial and error. With the knowledge now available a plan can be designed that provides not only for the organization of payment but also for the establishment and maintenance of high standards of service throughout the country.

The arguments advanced against the compulsory-health-insurance title of the Wagner-Murray-Dingell Bill and against the Maternal and Child Welfare Bill are many and varied. Those based on misinformation need no discussion here. Of the others, two deserve special consideration—the assertion that socialized medicine is just around the corner, and the assumption that so-called "political

medicine" is about to be imposed on the American people.

### SOCIALIZED MEDICINE

The term "socialization," and with it the term "socialized medicine," have been used in a shifting sense. The latter term actually has two quite dissimilar meanings.<sup>1</sup> It may denote a system of medical care organized on the basis of the political and economic theory of socialism. Such a program calls for public ownership of all facilities for medical care, with the abolition of nongovernmental ownership of institutions, for the employment of all professional personnel by public agencies, with the discarding of private practice, and for public administration of all health services, with elimination of nongovernment agencies. None of the bills under consideration propose the adoption of such a program.

The term "socialized medicine" may also mean a program of medical care organized for the purpose of adapting medicine to social needs and uses, with no regard to socialist doctrines and methods. In this sense, American medicine has been socialized for some time and to a considerable extent. At present, about three fourths of all beds in registered hospitals and probably about half of all clinics are in institutions built from tax funds and operated by local, state and federal agencies. Many and diverse socioeconomic groups are entitled to medical care at the taxpayers' expense. They include several million recipients of public assistance and many millions of self-supporting people, such as the veterans, merchant seamen, Indians and Eskimos, wives and infants of enlisted men, the medically needy and certain employees of the federal government. In the fiscal year 1943-1944, the total expenditures of tax funds for medical care of civilians amounted to at least \$900,000,000. The workmen's compensation acts, which are in force in all the states but one, require medical care to be furnished to those covered, and in 1943-1944 \$140,000,000 was spent for this purpose.

Taxation and insurance by law have been the two methods employed to finance medical-care programs in the past, and these are the very methods proposed for the organization of payment for medical care in the future.

The bugaboo of socialized medicine can frighten only those who mistake "social" for "socialistic." It is about time to stop fighting over terminology and to concentrate time and effort on the intricate task of working out the method of action that best promises to achieve the ends desired by all.

### POLITICAL MEDICINE

The second argument, which expresses a fear of political interference, if not political control, derives from the fact that in the past the selection of patients, the appointment of personnel,

methods of institutional administration were in some instances influenced by the desire to make friends, gain votes and reward favorite sons (and daughters) for faithful political activities. But the picture is not so black as some persons would have one believe. There are many examples of good government in the field of health administration. What is more significant, a growing number of agencies and communities have been making constant and determined efforts to clean their own houses and to eliminate the taint of political medicine.

The danger of political manipulation of a nationwide system of medical care cannot be lightly dismissed, but it can be averted. Let us now resolve to establish the tradition of good government in every community. If we fail in this task, we shall be admitting our unwillingness to exercise one of our precious constitutional rights and duties.

The major bills now under consideration have one element in common: they require all appointments to administrative positions to be made strictly on the basis of merit. Enactment of these measures will go a long way toward eliminating political interference in the administration of health services. It will afford a unique opportunity not only to deprive the last politicians of a happy hunting ground but also to generalize professional direction and supervision of professional matters.

#### VOLUNTARY HEALTH INSURANCE

Voluntary health insurance as an alternative to a compulsory program has been repeatedly recommended by the American Medical Association. In 1938, this organization announced its support of voluntary cash-indemnity insurance plans to cover, in whole or in part, the costs of emergency or prolonged illness. At the same time the Association recommended the expansion of workmen's compensation laws to provide for meeting the costs of illness sustained as a result of employment in industry, and thus endorsed the principle of required insurance for occupational diseases. In June, 1945, a so-called "Constructive Program for Medical Care" was adopted. One of its fourteen recommendations called for the development in or extension to all localities of voluntary sickness-insurance plans and provision for the extension of these plans to the needy under the principles already established by the American Medical Association. In December, 1945, the House of Delegates adopted a resolution calling for the nation-wide organization of locally administered prepayment medical plans sponsored by medical societies, which would, it was held, achieve all the objectives of the Wagner-Murray-Dingell Bill with far less expense to the people and would provide the highest type of medical care without regimentation. In February, 1946, the Board of Trustees issued a ten-point restatement of the Association's previously announced

fourteen-point program.<sup>4</sup> Standards for the acceptance of prepayment plans were established. A detailed plan for the development of the voluntary health-insurance program was announced to be in process of being worked out by a subsidiary organization known as Associated Medical Care Plans, and a new unit, the Division of Prepayment Medical Care Plans, was created to administer the voluntary plans under American Medical Association auspices.

The question is justified whether past experience warrants the belief that the American Medical Association can accomplish its objectives.

In 1945, about 2,600,000 persons were enrolled in so-called "medical-society plans." They accounted for approximately half the total membership of voluntary prepayment plans covering physicians' services. At a time when purchasing power was at an all-time high point, only an insignificant fraction of the population had decided to take advantage of the services offered by medical societies. Although the plans had been in operation for several years, some of them had failed to attract substantial numbers of subscribers. A case in point is the Western New York Medical Plan in Buffalo. This plan, established in 1940 and serving six counties with large populations, reported 40,000 subscribers as of the middle of 1945. With the exception of the programs in Oregon and Washington, the great majority of the medical-society plans offer extremely limited service. In 1945, two thirds of the persons enrolled were eligible only for surgical service in hospitals, and in many instances this service was restricted by ceilings on eligibility, the period of care or the total amount of cost. Only one person in seventeen was eligible for physicians' care at the home, office and hospital. In short, the majority of the medical-society plans are distinguished by the fact that exclusions exceed inclusions.

The eligibility requirements often contain a clause barring from the prepaid service persons and families with incomes above the comfort level. In some instances this level is set as low as \$1500 for a single person and \$2500 for a family. By establishing income limits, the majority of the medical-society plans have insured the poorer risks and disregarded the more favorable ones, thus acting contrary to the basic principle of insurance, have made the proposition unattractive to large families, management and labor and have placed the participating physicians in the unenviable position of investigators who have to check the family income to detect the patients who earn more than the limit.

The total cost of medical-society plans varies too widely to allow generalizations. The most successful plan, the Michigan Medical Service, in the middle of 1945 charged monthly rates of \$0.70, \$1.60 and \$2.25 for single subscribers, a family of two and families including all unmarried children up to nineteen years of age, respectively. These prepayments covered surgical service in the hospital and some

ancillary services. The physicians were free to make additional charges to those whose average annual income exceeded \$2000 in the case of single persons and \$2500 in the case of families. The Michigan Hospital Service, an outstanding Blue Cross Plan, charged monthly rates of \$0 80, \$1 80 and \$2 00, respectively, for ward care and \$1 00, \$2 20 and \$2 40 for semi-private care. To qualify for fairly complete hospital care and surgical service in the hospital, a single person had to make monthly prepayments ranging from \$1 50 to \$1 70, and a family of three or more had to pay in advance from \$4 25 to \$4 65 a month. These amounts equaled 1 2 and 1 4 per cent, respectively, of the income of single persons earning \$1500 a year, and 2 5 per cent and 2 8 per cent, respectively, of the annual income of families earning \$2000. It must be borne in mind that in 1945 an annual income of \$2000 was barely sufficient to cover the ordinary living expenses of the average city family with three members. Substantially higher rates and larger proportions of the income would be needed to extend the scope of the services. High prepayment rates, however, defeat their own purpose, since only a small fraction of the population can afford to pay them.

Most of the medical-society plans in actual operation discourage preventive medicine by excluding health examinations, by using deterrents, such as the deductible clause, and by confining medical care to catastrophic illness instead of trying to reduce, if not prevent, the occurrence of serious conditions by providing for early diagnosis and early treatment of disease. Limited in scope as those plans are, they cannot foster psychosomatic medicine. In many cases a premium is placed on surgery, little effort being made to establish and enforce standards covering the competence of those rendering the service for which payment is claimed.

In summary, many medical-society plans are organized merely for the purpose of making financial arrangements for the payment of doctors' bills. Little attention can be paid to the improvement of the quality of service. Judging from the numerous articles appearing in medical journals, many of the physicians participating in these plans are dissatisfied and are looking for "something else." Not a few show keen interest in cash-indemnity plans, although the shortcomings of this method have been proved time and again. In California, the Alameda County Medical Society, in opposition to the state medical society, recommends such a plan, and other county societies are said to have voiced their approval. In Wisconsin, the state medical society has just made an agreement with commercial insurance companies, which are to underwrite a limited indemnity policy, and many physicians are beginning to wonder why the medical society should "sell out" to companies organized for profit.

The policies adopted by medical societies in the past were dictated by necessity. The physicians draw-

ing up the prepayment programs entertained no illusions about the impossibility of establishing at reasonable cost a voluntary health-insurance program providing for complete service, offering unlimited free choice of physicians and paying the participating physicians on a fee-for-service basis. Societies that tried it failed. In California and Michigan, the medical societies had to drop their original full coverage contracts because of heavy financial losses. Between the Scylla of excessively high prepayment rates covering complete service and full payment for professional services and the Charybdis of moderate prepayment rates for complete service with extremely low fees for the physicians, the medical societies chose the only safe way — the offer of inexpensive and limited service to the subscribers and the promise of full payment to the physicians.

These facts, stated and commented on in countless publications in medical journals, indicate that the American Medical Association has taken on a Sisyphean task. It seeks to develop a satisfactory national health-insurance program by voluntary action, although the natural limitations of the voluntary method are well known. It desires to achieve the goal of country-wide organization, although the rank and file of the physicians are divided concerning the basic principles to be applied. Stormy debates are going on over the advantages and disadvantages of cash-indemnity plans and service plans, of combination and separation of professional services and hospitalization, of complete coverage and partial coverage of service, of rigid and liberal eligibility requirements and of individual practice and group practice. The American Medical Association believes that it can make the enactment of a health-insurance law superfluous by promising something better in the future, although a broad and balanced health program is needed now.

\* \* \*

Whatever the fate of the various health bills may be, the wide discussion of the proposals will set in motion many changes in community planning for health services in general and for more effective organization of hospital and professional services in particular.

The problems we are now facing are highly complicated. Their solution requires accurate analysis of facts, correct appraisal of existing medical-care programs, fearless use of reason, constructive criticism of any proposal for the improvement of health services and single-mindedness in carrying out what appears to be a sound policy and one that is in accord with democratic ideals.

As Franklin Delano Roosevelt said in his Jefferson Day Address, written shortly before his death: "The only limit to our realization of tomorrow will be our doubts of today. Let us move forward with strong and active faith."

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## INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM IN INFECTIOUS MONONUCLEOSIS\*

## A Report of Two Cases

CAPTAIN JOHN DER SLADE, M C, A U S

**I**NFECTIOUS mononucleosis is generally regarded as a benign disease having a uniformly good prognosis. In the majority of cases this belief is substantiated, but in occasional cases this disease causes permanent damage and sometimes seriously threatens life.

The clinical features of infectious mononucleosis have been described in detail<sup>1-6</sup> and there are numerous articles on the hematological findings.<sup>1, 2, 5, 7-10</sup> There have, however, been relatively few reports dealing with the abnormalities of the central nervous system sometimes encountered.

The first case of involvement of the central nervous system in infectious mononucleosis was reported by Johansen<sup>11</sup> in 1931. His patient presented meningismus, drowsiness, impaired memory, dysarthria and weakness, in addition to the usual anginous type of infectious mononucleosis. In the same year Epstein and Dameshek<sup>12</sup> reported a comparable case in which there was ptosis of the right eyelid, a positive Kernig sign, a transiently positive Babinski sign, blurred vision and delirium. Both these patients made complete recoveries within two months.

In 1935, Fladelius<sup>13</sup> reported a case of infectious mononucleosis complicated by diplopia due to paresis of the left inferior rectus muscle, associated with stiff neck, headache, exaggerated knee jerks and questionable plantar reflexes. Improvement was gradual, with complete recovery in eighty days. In the following year, Sucher and Schwarz<sup>14</sup> described 2 severe cases in which death seemed imminent. The first patient presented drowsiness, horizontal nystagmus, right oculomotor paralysis, ataxia, adiadochokinesis and positive Babinski, Oppenheim and Kernig signs. Improvement in the third week was followed by relapse in the fourth week, with convulsions, left hemiplegia, cyanosis and pulmonary edema. Recovery was effected after seventy-five days. In the second case there was coma, opisthotonus, severe convulsions, left hemiplegia and pulmonary edema, but recovery was rapid, being complete in three weeks.

The second American case was reported in 1937 by Davidsohn.<sup>15</sup> This patient had coma and con-

vulsions. It is noteworthy that this was the first case of encephalitis due to infectious mononucleosis to be proved by the heterophil agglutination reaction, the diagnosis in the previous cases having been based on the combination of lymphadenopathy, lymphocytosis and the finding of the typical cells in blood smears.

In 1937, Gsell<sup>16</sup> reported 5 cases showing involvement of the central nervous system. One patient developed an optic neuritis, the remnants of which were visible a month later. Transient facial paralysis was present in 2 cases. In one of these, a right facial paralysis was followed a week later by involvement of the left facial nerve. In the other case, a right facial palsy lasting a week occurred a month after apparent recovery from an otherwise typical infectious mononucleosis.

Cases of infectious mononucleosis with involvement of the central nervous system have been reported more frequently in recent years. Various parts of the nervous system are primarily involved in different patients, so that the clinical picture may be that of meningitis,<sup>17-19</sup> encephalitis,<sup>20-22</sup> meningo-encephalitis,<sup>23</sup> encephaloneuronitis,<sup>24</sup> encephalomyelitis<sup>25</sup> or neuronitis.<sup>26, 27</sup>

The time interval between the onset of infectious mononucleosis and the development of neurologic abnormality is quite variable. If one excludes headache as a significant symptom, it is seen that involvement of the central nervous system may be apparent as early as the first day of illness<sup>12</sup> or be delayed until the thirty-first day,<sup>16</sup> but it usually occurs in the second week of illness. The signs and symptoms depend on what portion of the nervous system is attacked, and there therefore is considerable variation from one case to another. Table 1 lists the signs and symptoms recorded in the cases reviewed and gives the number of cases in which each finding occurred.

The cerebrospinal-fluid findings parallel the neurologic process, a pleocytosis accompanying meningitic signs and a normal or slight increase in cell count is found in neuronitis and in purely encephalic cases. The cells are predominantly

\*From the American Air Force Regional and Air Debarkation Hospital, Hamilton Field, California.

†Headache was present in the majority of cases, but is so frequent in apparently uncomplicated cases<sup>28</sup> that it is of little diagnostic value unless it is unusually severe.

lymphocytes. The protein content is usually increased, and the Pandy test may be strongly positive,<sup>24</sup> although it is sometimes negative.<sup>12</sup> The mastic curve is variable.<sup>16, 24</sup>

Little is known of the actual lesions in these cases, because there has been such a paucity of material for histologic study. Ziegler<sup>29</sup> has recently reported a case of infectious mononucleosis in which death resulted from rupture of the spleen. At autopsy, focal lesions were found in the liver and kidneys, with mononuclear infiltration, proliferation of retic-

TABLE 1 *Signs and Symptoms of Involvement of the Central Nervous System in Infectious Mononucleosis*

SIGN OR SYMPTOM	NO OF CASES	SIGN OR SYMPTOM	NO OF CASES
Headache	30	Absent abdominal reflexes	3
Stiffness of neck	17	Nystagmus	3
Positive Kernig sign	8	Opisthotonus	3
Lethargy	7	Paralysis of serratus anterior	2
Muscle twitching	6	Diplopia	2
Dizziness	6	Positive Oppenheim sign	2
Dysarthria	6	Oculomotor paralysis	2
Positive Babinski sign	5	Hemiplegia	2
Facial paralysis	5	Stupor	2
Nausea	5	Coma	2
Photophobia	4	Delirium	2
Convulsions	3	Optic neuritis	2
Ptosis	3	Absent cremasteric reflexes	2
Ataxia	3	Anosmia	1
Dysphagia	3	Blurred vision	1
Vomiting	3	Impaired memory	1
Adiadokinesis	3	Paraplegia	1
Hyperesthesia	3	Quadriplegia	1
		Paralysis on upward gaze	1

\*Prepared from the available data of 32 cases reviewed (including the author's cases)

ulocytes and necrosis suggesting an acute infectious granulomatous process. Ziegler states that the disease appears to be a generalized infection, with specific localization in one or more of the tissues or organs of the body.

In 1939, Thomsen and Vimtrup<sup>30</sup> reviewed 500 cases of infectious mononucleosis seen in Copenhagen and described 6 fatal cases. In 4 of these there was no associated disease, death being ascribed to infectious mononucleosis, in all 4 cases death was attributed to respiratory paralysis. In 1 case an autopsy was performed and the histologic study showed severe degeneration of the cells in the region of the respiratory center. With the notable exception of these cases, there have been no deaths from damage to the central nervous system by infectious mononucleosis.

Permanent residuums due to infectious mononucleosis are unusual, but they have been reported by Marchal<sup>31</sup> (anosmia) and Saksena<sup>27</sup> (paralysis of serratus anterior).

The following case reports illustrate the encephalomyelitic and encephalomyelitic types of infectious mononucleosis. In both these patients there was evidence of permanent damage to the nerve tissue. The second case is also remarkable in that it represents one of the few reported cases of infectious mononucleosis in a Negro.<sup>32, 33</sup>

**CASE 1** A 31-year-old man was admitted to the hospital on August 25, 1944, complaining of headache, chills and fever. He had previously been well in all respects until 3

days prior to admission, when he developed swelling below the left ear, malaise and a fever while on a railroad journey. During the next 2 days these symptoms increased in severity, headache occurred, and the patient was seen by a medical officer, who prescribed sulfonamide tablets. The patient took a total of 4 tablets within a period of 12 hours, but the fever, headache and malaise increased and were accompanied by chills, so that as soon as the train reached its destination he was admitted to this hospital. The past history and family history were noncontributory.

Physical examination on admission showed an acutely ill, flushed patient perspiring freely. The temperature was 103°F, the pulse 100, and the respirations 35. The significant findings were diffuse injection of the conjunctivae, slight reddening of the throat, and moderate enlargement of the left postmandibular lymph node, which was nontender. The blood pressure was 105/80. The heart and lungs were normal. The neurologic findings were normal.

The laboratory data are given in Table 2. Blood Kahn reactions were repeatedly negative, as were x-ray studies of the chest and skull. Serum from blood samples taken on September 11 and October 4 were sent to the Army Medical School, where they were found to be negative for the viruses of Western equine encephalitis, St. Louis encephalitis and lymphocytic choriomeningitis.

The temperature spiked to 103°F on the 2nd and 3rd days and then dropped to normal, where it remained on September 1 and 2. It rose to 102°F on September 3, and there was a low grade fever until September 8, when the temperature became normal and remained so. The respiratory rate was normal after the 1st day, and the pulse was proportionate to the temperature.

On symptomatic treatment, the patient seemed to improve, but on August 30 considerable increase in the lymphadenopathy was noted, the cervical, supraclavicular, epitrochlear and popliteal nodes being palpable. On the night of September 2, the 11th day of the illness, the patient developed some difficulty in speech and chewing and stated that his right cheek felt as though it were asleep. These symptoms progressed and extended, coincident with the rise in temperature, and on September 4 examination showed slurred speech, inability to chew, complete bilateral facial paralysis and loss of the gag reflex. The eyes turned upward and slightly to the left when the patient attempted to close them, and there was paralysis of upward gaze without loss of convergence. The right abdominal reflex was sluggish, and the right cremasteric reflex was absent. The sensorium, deep reflexes and cerebellar functions were normal.

The chief complaint at that time was an overwhelming feeling of tiredness. The patient's condition was considered quite serious. Suction apparatus was required to keep the throat and air passages clear, and special nurses were assigned. An additional finding, the true significance of which was in question because of its close similarity to a hysterical tic, was the apparently involuntary sucking, smacking and mumping noises that the patient made with his mouth every few seconds. This phenomenon persisted for 1 week and then gradually disappeared. The gag reflex returned on September 6, and by the next day the lymphadenopathy was generally diminished and the marked faugue had subsided.

During the next 3 days the patient complained of sharp pains at odd intervals in the posterior cervical and sternocleidomastoid muscles, weakness of which was demonstrated for 2 months. Between September 8 and 11, a small patch of diminished sensitivity to pain developed on the neck just below the ear, first on the right and later on the left. This persisted until September 21. The chewing and swallowing gradually improved, so that by September 15 the patient was eating soft foods without assistance. It was not until September 29 that he was able to eat toast, since his tongue, lips and masseters were so poorly co-ordinated that he frequently bit his lip, tongue or cheek. His speech improved considerably, although it remained explosive at times and vocalization was preceded by inspiratory stridor.

On October 19, the patient was transferred to a general hospital. The significant findings on October 21 were as follows: complete facial paralysis, loss of taste over the anterior two thirds of the tongue, hippus of both pupils, loss of pain and temperature sense over the distribution of the trigeminal nerves, generalized muscle weakness, cogwheel rigidity of the arms, marked weakness of trapezius and sternocleidomastoid



muscles, loss of the left superficial abdominal and cremasteric reflexes, with diminution on the right, and a hopping gait. In November, the patient was transferred to another general hospital. Examination on November 12, the 82nd day of the illness, showed numerous abnormalities. The left leg dragged on walking, and the patient tended to fall toward the left with his eyes open or closed. There was adiadochokinesis, paralysis of upward gaze, loss of pain, vibratory sense, temperature perception and light touch throughout

venereal disease. The only previous hospitalization was in September, 1944, and was due to scabies and pityriasis rosea. At that time peripheral arteriosclerosis was also diagnosed, being manifested by intermittent claudication and x-ray evidence of calcification in the femoral and popliteal arteries. Except for a mild degree of intermittent claudication which had been present for 2 or 3 years, the patient was in apparent good health until 2 weeks prior to admission, when he developed coryza, mild malaise and generalized aching, with

TABLE 2 Laboratory Data in Case 1

Date	RED-CELL HEMOGLOBIN		WHITE CELL COUNT	BLOOD DIFFERENTIAL COUNT				HETEROPHIL TEST	CELLS	SPINAL FLUID TOTAL PROTEIN	HETEROPHIL TEST
	count	gm /100 cc		Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %				
	$\times 10^6$		$\times 10^3$					serum dil	per cu mm	mg /100 cc	
Aug. 26	4.91	14.7	6.2	72	22	5	1	1:56			
Aug. 29			11.6	25	69	5	1				
Aug. 30			15.1	20	76	2	2				
Aug. 31								1:112			
Sept. 4									4	91	
Sept. 5			17.8	19	76	5	0	1:112			
Sept. 6									3		
Sept. 14	4.80	15.6	10.2	20	72	7	1	1:896			Neg
Sept. 26			9.9	40	54	3	3	1:7			
Oct. 7			9.5	30	64	2	1				
Nov. 16									0	44	
Nov. 17	4.76	14.5	8.0	41	58	0	1				

the face, complete bilateral facial paralysis, bilateral weakness of the trapezius muscle, generalized motor weakness throughout the body, slightly greater on the right side than on the left, generalized contraction of the visual fields, somewhat more marked on the left than on the right, and athetoid movements of the hands and fingers. Electroencephalograms were made on November 20 and December 1. These were interpreted as mildly abnormal tracings consistent with diffuse encephalopathy. Despite prolonged hospitalization, physiotherapy, abundant vitamin therapy and a nutritious diet, no additional improvement was obtained, and the patient was discharged from the Army on December 27. In March, 1945, about 200 days after the onset of his illness, the patient reported that his speech was somewhat better

some tingling in the hands, arms and face. This group of symptoms persisted without appreciable change until admission. Physical examination revealed a well developed and well nourished Negro in no apparent discomfort. The temperature was 98°F, the pulse 88 and the respirations 16. The blood pressure was 114/76. Numerous small oval patches of dark-brown pigmentation were scattered irregularly over the trunk and extremities. Peripheral vessels were compressible but easily rolled beneath the fingers. There was moderate enlargement of the anterior and posterior cervical and axillary lymph nodes bilaterally and slight enlargement of the inguinal nodes bilaterally, with no tenderness of any of the nodes. There was bilateral pes planus. No note was made of the reflexes. The laboratory findings are shown in Table 3.

TABLE 3 Laboratory Data in Case 2

Date	RED-CELL HEMOGLOBIN		WHITE-CELL COUNT	BLOOD DIFFERENTIAL COUNT				HETEROPHIL TEST	SPINAL FLUID TOTAL PROTEIN	
	count	gm /100 cc		Neutrophils %	Lymphocytes %	Monocytes %	Eosinophils %		cells	mg /100 cc
	$\times 10^6$		$\times 10^3$					serum dil	per cu mm	
Nov. 24	4.60	14.4	4.4	58	40	2	0			
Nov. 27	4.68	14.4	7.9	54	41	5	0			
Dec. 1	4.51	14.4	6.0	58	36	4	2	1:56		
Dec. 4									1	43
Dec. 6			6.5	60	30	8	2	1:112		
Dec. 9	4.57	14.4	6.1	63	30	7	0	1:56		
Dec. 13									2	44
Dec. 19			5.9	45	55	0	0	1:56		
Dec. 26			4.1	36	60	4	0			
Dec. 29			4.6	63	35	4	0			
Jan. 9			4.8	62	27	8	3			
Jan. 30	4.19	13.5	11.7	73	16	7	4			
Feb. 12	3.91	12.9	4.2	65	27	6	2	Neg		
Feb. 21	4.70	14.7	4.9	52	40	6	2			
Mar. 29	4.75	15.0	5.1	52	48	0	0			

and that he could smile slightly, but that he still had loss of taste, numbness of the face and inability to look upward and had developed a high-pitched whistle in the right ear.

CASE 2. A 36-year-old Negro entered the hospital on November 28, 1944, complaining of frontal headache, malaise and generalized aching. The family history was not remarkable except that a maternal uncle had died of hypertensive heart disease. The past history included measles, chicken pox and whooping cough in childhood, without complications or sequelae, uncomplicated mumps in 1926, malaria in 1923, with several recurrences, the last being in 1927, and tonsillectomy in 1924. There was no history of head trauma or

The blood Kahn reaction was negative, as were x-ray studies of the skull, sinuses and chest. On bed rest the patient became more comfortable, but on December 1 the frontal headache became severe and he complained of numbness of the chin. On the same day he noticed some difficulty in chewing, could not control the movements of his tongue and developed weakness of the arms and legs. These symptoms continued, with accentuation of the headache at night, so that by December 4 the following physical findings were apparent: a completely expressionless face with inability to smile, whistle, frown or close the eyes completely, Bell's phenomenon, in which the eyes roll upward when the patient tries to close his eyes, slight ptosis of the eyelids, hyperesthesia over the temporomandibular region,

anesthesia of the chin from the mental foramen of one side to that on the opposite side, dysarthric, slurred speech, absence of the gag reflex, paresis of the masseters and pterygoids, diminished muscle reflexes in the upper extremities, absent knee jerks and ankle jerks, diminished superficial abdominal and cremasteric reflexes, a normal plantar reflex, and adiadokokinesis.

The temperature was normal except on December 1 and 2, when it reached 100 and 99.6°F, respectively. During the next few days the gag reflex returned, and enough strength returned to the masseters so that the patient could eat semisolid food. The frontal headache persisted, being mild during the day but severe at night. Considerable tenderness of the facial muscles was also noted during this phase. The generalized lymphadenopathy was considerably reduced by December 10 and became unnoticeable by December 14.

On December 15, the patient complained of increased aching of the muscles of all extremities. Examination at that time showed generalized muscle tenderness and weakness, with marked weakness of the biceps, triceps, thigh extensors and hamstring muscles, the paresis being somewhat more pronounced on the right than on the left. No further change was noted until December 26, by which time the headaches had ceased. By January 3, 1945, the patient had recovered sufficient strength in the right upper extremity to write a short letter. This was the first objective evidence of improvement.

On January 4, a right-sided foot drop was observed, this had probably been present previously but had not been noticed until the patient was allowed out of bed. On the following day some improvement in the muscle strength of the extremities was apparent, the muscle soreness becoming less as the tone improved. From this date onward the patient made gradual, albeit limited, improvement. By January 15 he had regained some use of the facial muscles, being able to smile slightly and raise his eyebrows. The chin anesthesia was also diminished by this time, and the speech was better, although still somewhat thick. The gait was of the waddling and shuffling type, with a right-sided foot drop. On January 18, the superficial abdominal reflexes were found to be brisk. The cremasteric reflexes were still abnormal, however, in that stimulation of the medial surface of the thigh resulted in lower abdominal reflex spasm but caused no contraction of the dartos muscle. Graduated physiotherapy was begun on January 19, and subsequent improvement was gratifying, the speech becoming practically normal by January 23, the facial expression returning in some measure and the foot drop becoming unnoticeable by January 27. Ophthalmologic examination was negative except for a slight contraction of both visual fields, which remained stationary. Further progress was slow and of limited extent. Except for the first few days of hospitalization, when the patient was drowsy and apathetic, he was mentally alert and cheerful throughout his illness.

General examination on March 17 showed some residual facial weakness, with inability to frown or whistle, and moderate weakness of the pterygoids and temporal muscles. The sternocleidomastoid muscles and those of the extremities were generally soft and flabby, with poor tone and strength, the reflexes in the upper extremities were hypoactive. Knee jerks and ankle jerks were absent, and there was a waddling gait. Finger-to-finger and heel-to-heel tests were well performed.

Physical examination on April 6 showed slight improvement in muscle strength of the extremities and sternocleidomastoids, but the thigh and calf muscles were still tender on deep pressure and squeezing. Stiffness of the upper lip was still apparent on talking and in drinking from a glass, and the gait was shuffling. There was a fine tremor of the fingers and some tremor of the arms and legs when placed on tension. The muscle reflexes of the upper extremities were quite hypoactive, the knee jerks and ankle jerks were absent, but the superficial abdominal and cremasteric reflexes had become active and normal. At that time, 5 months after the onset of illness, it was believed that complete recovery was unlikely and the patient was discharged from the Army on April 14.

#### DISCUSSION

At the time of admission of both these patients the clinical impression was that of infectious mononucleosis. When the paralytic symptoms appeared,

the differential diagnosis broadened. One of the diseases considered was poliomyelitis. No report on sheep-cell agglutination tests in the acute stages of this disease is to be found in the literature, but Hammon and Lawson<sup>24</sup> at the University of California performed Paul-Bunnell tests on serums from 13 patients with paralysis due to poliomyelitis and found that no titer was higher than 1:28.

Clinical observations of these cases support the concept of infectious mononucleosis as a generalized infection with specific localization in one or more of the tissues or organs of the body.<sup>29</sup> In the cases described above there was apparently diffuse and spotty involvement of the nervous system. The clinical picture is similar to that produced by viruses of other diseases and suggests that this too may be a virus infection.

The recognition of disease of the central nervous system due to infectious mononucleosis is a simple matter if one is acquainted with the knowledge that it occurs. The actual incidence of such complications is difficult to estimate and is probably quite low. The important thing, however, is the realization that infectious mononucleosis is not always a benign disease. Patients with this disease should not be dismissed lightly, but deserve careful medical observation and attention.

#### SUMMARY

A review of the literature indicates that infrequent cases of infectious mononucleosis causing disturbances in the central nervous system have been observed.

Cases of fatal respiratory paralysis due to this disease have been recorded.

Two cases are reported in which infectious mononucleosis resulted in such severe damage to the central nervous system that the patients were declared unfit for further military service.

It is emphasized that infectious mononucleosis is a potentially serious disease, worthy of respect as a generalized virus infection that may threaten life.

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MEDICAL PROGRESS

FLUORINE AND DENTAL CARIES

VLADO A. GETTING, M.D., D.R.P.H.\*

BOSTON

PREVALENCE OF DENTAL CARIES

DENTAL caries is perhaps the most widespread of all diseases of mankind and is one from which very few persons escape, especially in civilized races. It has been demonstrated that a positive correlation exists between the primitive (carnivorous) diets of Eskimos in Alaska and their relative freedom from dental decay.<sup>1</sup> A high prevalence of dental decay, however, is found among Eskimos who live in cities and consume a civilized diet. Practically every adult and almost every child over six years of age has suffered from dental defects.<sup>2</sup> These defects often induce a train of related maladies that could have been prevented by proper dental care. Dental diseases are not limited to any group and attack all persons, regardless of age, sex, geographical location or economic status.

Dental caries is the destroyer of most teeth that are lost by persons under thirty, thereafter pyorrhea assumes first rank as the cause of loss of teeth. Caries begins as soon as a child has teeth. Over ninety-five per cent of children ten years of age have one or more decayed permanent teeth. By the time the child reaches eighteen, nine permanent teeth, on an average, have become decayed and several extractions have had to be made. The loss of certain teeth upsets the proper alignment of others and brings about malocclusion and predisposes to pyorrhea, the prime cause of loss of teeth in later life. Moreover, diseased teeth and gums may cause disease, directly or indirectly, in adjacent as well as other parts of the body.

Once a defect is produced by decay, evidence of

its existence is never obliterated.<sup>3</sup> It is therefore possible by direct examination to determine what has happened to teeth in the past. The permanent teeth with defects caused by present and past attacks of caries are classified in three groups—decayed teeth, those with open carious lesions requiring treatment by fillings, missing teeth, those already extracted or requiring immediate extraction because of extensive destruction of caries, and filled teeth, those previously carious but with evidence of treatment in the form of fillings.<sup>4</sup> By common usage and for the purpose of brevity, teeth so affected are collectively designated by the symbol "DMF" (decayed, missing and filled).

Because of the characteristic accumulation of caries stigmas with increasing age, the increment in the number of DMF teeth or of DMF surfaces per year per person may be taken as a measure of the incidence of caries. The prevalence of caries may be measured in several ways—by the ratio of the number of persons per 100 population having one or more DMF teeth, the total DMF teeth per person, and the number of DMF surfaces per person, which gives a fuller comparison than either of the foregoing, since each tooth may be attacked on several surfaces.

EPIDEMIOLOGY OF DENTAL CARIES

Age

One of the most significant factors associated with increased dental caries is age. Studies made in 1940 by Klein and Palmer<sup>5</sup> on 6200 children in Hagerstown, Maryland, and in the same year by Sloman and Sharp<sup>6</sup> on 6300 high-school children in San Francisco yielded definite evidence of the accumulative destruction caused by dental caries. At six

\*Commissioner, Massachusetts Department of Public Health and lecturer in public health practice, Harvard School of Public Health

years of age, 15.9 per cent of the Hagerstown children had one or more DMF teeth, the percentage increased each year until by eighteen years of age it was 96.6 per cent. The San Francisco high-school children showed an increase from 91.0 per cent at the age of thirteen to 97.2 per cent at eighteen. If the second method of analysis is used, the number of DMF teeth per child in the Hagerstown group increased from 0.29 at the age of six to 9.25 at nineteen, and that in the San Francisco children increased from 3.8 at the age of twelve to 8.3 at eighteen. When the same method of comparison was applied to an adult population in New York City in 1939 by Hollander and Dunning,<sup>7</sup> it revealed a steady increment of tooth destruction with advancement in age, for example, at twenty to twenty-four years there were 15.82 DMF teeth per person, at forty to forty-four years, 21.61, at fifty to fifty-four years, 22.36, and at sixty to sixty-four years, 23.37. If the third method of comparison (DMF surfaces per person) is applied to the Hagerstown and New York City data, it is found that there was a constant increase of tooth decay with advancing age. At six years of age the Hagerstown children averaged 0.38 DMF surfaces per child, at ten years 4.87 and at fifteen years 13.35, whereas in adults in New York City the average increased from 31.52 at the age of twenty to twenty-four to 70.09 at the age of sixty-five and over.

### Sex

Several observers<sup>8-11</sup> have noted a greater prevalence of dental caries among females than among males, but this is probably due to the earlier eruption of the permanent teeth rather than to a predisposition to the formation of caries. Females have a greater amount of dental decay than do males of the same age. In 1938, however, Klein and Palmer<sup>12, 13</sup> demonstrated that this difference is also due to the fact that permanent teeth erupt earlier in girls than they do in boys. Actually, therefore, if a comparison of the age of the teeth is made for the two sexes, there is no significant difference in dental decay until the age of fifteen years. Thereafter there is a gradual increment of dental decay in females with advancing age.

### Race

Only scattered data on the difference in the prevalence of caries observed in different races are available. They indicate that race is a significant factor. Negro children have lower rates of DMF teeth per person than do white children,<sup>3</sup> the difference increasing with age. Thus, at ten years of age, in the white children of Hagerstown and Baltimore<sup>4, 5</sup> the rate was 2.5, compared with 1.6 in Negro children of the same communities. In Indian children of the same age examined by Klein and Palmer<sup>14</sup> the rate was 1.3, whereas in Navajo children of this age it was 0.5. At fifteen years of age the rate for

Hagerstown white children was 6.6, that for San Francisco white children was 6.5, that for Hagerstown Negro children was 4.1, and that for Navajo children was 3.1. In other words, the white children had about one and a half times as many decayed, missing or filled permanent teeth as did the Negro children and twice as many as did the Navajo children.

### Familial Susceptibility

Several investigators<sup>15-20</sup> have studied familial susceptibility to dental caries. Although their findings indicate a significant difference between different families, it is not clear whether these observed differences are in reality due to inherited (Mendelian) factors or whether they are not more probably due to environmental factors, such as family eating habits, consumption of candy, poor economic status and other factors that are common to the members of the same household.

Klein and Palmer<sup>21</sup> studied 4400 white elementary-school children in Hagerstown and found 117 with extreme susceptibility to caries and 184 with immunity to it. The susceptible children had 182 siblings, whereas the immune children had 306, all of whom had been examined. Studies of these records revealed that the tendency toward caries of the siblings of immune children was about half that of the siblings of susceptible children.

### Economic Status

The literature tends to suggest that economic status does not markedly affect the prevalence of caries, although the amount of dental work is related directly to the income of the family.<sup>22-24</sup> Klein and Palmer<sup>25</sup> studied the caries prevalence rate for 200,000 children in forty New Jersey communities. They concluded that the intrinsic tendency of children to experience attacks on the permanent teeth by caries does not depend on the economic status of the community in which they live. The volume of dental care in the form of fillings in the permanent teeth, however, markedly increased with improvement in the economic level of the community, the odontothanatotoxic rate (the number of permanent teeth extracted and indicated for extraction per 100 children) diminishes as the economic level rises.

Conclusions contrary to these reports were reached by Hyde,<sup>26</sup> who examined inhabitants of Massachusetts at the Boston Armed Forces Induction Station. The incidence of caries (DMF teeth) per person was highest in the most prosperous communities and lowest in the poorest communities. The English and Irish had the greatest amount of dental decay, whereas the Negroes and Chinese had the least. Three times as many selectees from Irish communities as from Portuguese or Russian (Jewish) communities were rejected for dental defects. The evaluation of the influence of economic factors on

dental caries must in the final analysis await a detailed study of other factors that are usually related to economic ones, such as diet and outdoor activity

### Geographical Location

There appears to be a definite correlation between the prevalence of dental caries and several factors involved in geographical location. These factors pertain not only to certain locations within the United States but also to geologic formations and

believes that areas having high annual total hours of sunshine have less caries than do areas with fewer hours of sunshine. Nizel and Bibby<sup>29</sup> are convinced that geographic variations have a definite influence on the prevalence of dental caries, as was demonstrated on examination of 22,117 soldiers in Camp Edwards, Massachusetts. Many earlier observers — Lewis<sup>30</sup> in 1865, Britten and Perrott<sup>31</sup> for draftees in World War I, Ferguson<sup>32</sup> for naval recruits and Senn<sup>33</sup> for aviation cadets in World War II — have shown that New Englanders had a higher exemp-

TABLE 1 *Prevalence of Caries in Draftees and Recruits*

STATE	DRAFTEES <sup>30</sup> 1863-1864		DRAFTEES <sup>31</sup> 1918		NAVAL RECRUITS <sup>32</sup> 1934		SELECTEES <sup>33</sup> 1943	
	RATE OF REJECTION FOR LOSS OF TEETH	ORDER OF PREVA- LENCE†	RATE OF REJECTION FOR DEFECTIVE AND MISSING TEETH	ORDER OF PREVA- LENCE	AVERAGE NO OF DECAYED AND MISSING TEETH PER RECRUIT	ORDER OF PREVA- LENCE†	AVERAGE NO OF DECAYED AND MISSING TEETH PER SELECTEE	ORDER OF PREVA- LENCE†
	<i>per 1000</i>		<i>per 1000</i>					
Alabama			9 30	39	3 50	24†	10 07	22
Arizona			7 29	42	6 00	16*	8 87	37
Arkansas			2 90	49	3 00	27	7 76	44
California			14 02	31	6 00	16*	8 93	35
Colorado			10 24	37	6 00	16*	8 32	40
Connecticut	26 53	3	36 52	8	12 54	1	10 97	14
Delaware	7 62	15	35 02	9	9 70	9*	17 05	1
Florida			23 03	15	3 60	23	8 79	39
Georgia			21 19	19	3 40	25†	9 99	26
Idaho			16 58	27	6 00	16*	11 59	11
Illinois			17 48	25	9 25	10	10 12	20
Indiana			9 47	38	4 38	19	10 18	19
Iowa			12 76	35	4 10	21	9 31	29
Kansas			3 89	48	4 00	22*	7 81	43
Kentucky	10 98	13	8 75	41	4 30	20	10 02	25
Louisiana			23 71	13	4 00	22*	9 20	31
Maine	10 21	14	79 45	5	10 20	8*	15 96	2
Maryland	16 57	11	21 28	18	9 70	9*	10 62	15
Massachusetts	34 87	1	78 82	5	12 20	2	12 06	8
Michigan	13 11	12	34 50	10	7 14	13	10 27	18
Minnesota	22 03	7	20 06	21	9 10	11	10 06	23
Mississippi			13 31	33	3 40	25†	8 92	36
Missouri			6 52	44	4 40	18	10 11	21
Montana			23 17	14	6 00	16*	8 84	38
Nebraska			6 13	45	6 80	15	9 14	32
Nevada			13 45	32	6 00	16*	7 90	42
New Hampshire	25 05	5	92 03	2	10 20	7	12 15	7
New Jersey	20 19	9	52 38	6	10 30	6	12 43	6
New Mexico			5 93	46	6 00	16*	7 67	45
New York	27 56	2	43 13	7	10 84	5	13 88	4
North Carolina			17 07	26	5 30	24†	8 95	33
North Dakota			19 02	22	6 00	16*	10 39	17
Ohio			14 62	30	10 53	6	11 70	10
Oklahoma			6 95	43	4 00	22*	7 37	46
Oregon			27 38	12	6 00	16*	12 62	5
Pennsylvania	25 70	4	29 08	11	11 40	3	10 46	16
Rhode Island	22 46	6	79 26	4	11 00	4	15 39	3
South Carolina			18 81	23	4 00	22*	9 23	30
South Dakota			20 91	20	5 30	17	9 64	28
Tennessee			11 04	56	3 20	26	8 95	34
Texas			5 91	47	4 00	22*	6 44	48
Utah			18 71	24	6 00	16*	9 89	27
Vermont	20 57	8	102 85	1	10 20	8	11 00	13
Virginia			21 33	17	4 00	22*	8 31	41
Washington			27 91	16	6 00	16*	11 23	12
West Virginia			13 21	34	7 50	12	10 05	24
Wisconsin	18 87	10	16 03	29	7 00	14	11 98	9
Wyoming			9 28	40	6 00	16*	6 69	47
District of Columbia	5 39	16	16 15	28	9 70	9*		

\*Owing to the small number of recruits from certain areas those from contiguous states were tabulated together and each state was given the same rate.

†Figure happened to be the same for these states.

‡States are arranged in the order of descending prevalence.

climatologic differences. Mills,<sup>27</sup> after studying the prevalence of caries in different latitudes, concluded that rates are highest in the northern and lowest in the southern areas of the country. In latitudes 25 to 26° the prevalence rates of DMF teeth were under 300 per 100 boys, whereas in latitudes 37 to 48° they were above 300. The rate increased by about 15 units for each degree farther north. East<sup>28</sup>

tion rate because of dental defects than did draftees from other sections of the country. Nizel and Bibby believe that the consistent repetition of this phenomenon over a period of eighty years eliminates all possibility of chance and establishes geographic variation in the prevalence of dental decay. The geographic prevalence of caries in draftees and recruits is summarized in Table 1.

The role of the mineral composition of public water supplies in relation to dental caries has been extensively studied by many authors, especially Dean<sup>34</sup> and East<sup>35</sup>. Both positive and negative relations between hardness of water and prevalence of caries have been reported by different investigators. East<sup>36</sup> offers evidence that users of hard water have less caries than do users of soft water. It has, however, been pointed out by Dean<sup>37</sup> and many others that this phenomenon is not the result of hard waters but rather the presence of fluorides in them. The role that fluorine plays in the prevention of caries is discussed in detail later in this paper. Nizel and Bibby, however, noted that caries is prevalent in regions with podzol and gray-brown podzolic soil and that wide variations in susceptibility to it occur in association with the red and yellow, chernozem and chestnut and prairie-soil regions of the south and the midwestern states. Finally, these authors urge more extensive investigation of soils in relation to dental caries, pointing out that there may be other rare elements besides fluorine that influence the incidence of dental decay.

### Diet

McCollum,<sup>3</sup> after examining the literature relating to the etiology of dental caries during recent years, concluded that there is an agreement among authors that carious lesions are caused by acid decomposition of the tooth enamel and subsequently the dentin, associated with proteolytic destruction of the organic substance of the tooth. There is unanimity of opinion that caries is restricted to persons and animals that have a liberal carbohydrate diet, whereas carnivorous men and animals do not suffer from this disease. Dental caries does not attack the surfaces of teeth indiscriminately but occurs only at sites that favor the lodgment of food particles or on surfaces of the enamel that harbor mucinous plaques. In these sites, acid is formed by fermentation of carbohydrates by micro-organisms and is protected by the plaques against being washed away by saliva or neutralized by salivary alkalinity.

Faulty structure in the enamel may cause the lodging of food particles in fissures and pits and thereby predispose to the formation of dental caries. The filling of these defects prior to decay is known as prophylactic odontotomy and has proved to be an effective means of prevention of caries. Such defects, however, may be the result of dietary deficiency. When, owing to vitamin A deficiency, the enamel-forming cells are injured, enamel prisms that are less dense than normal ones or are incomplete as to length and imperfectly fitted together form defective enamel. In severe cases vitamin A deficiency causes hypoplastic teeth, characterized by thin enamel deficient in hardness, in milder deficiency there may be pitting.

Vitamin D deficiency, with the disturbance of calcium and phosphate metabolism of rickets, may

cause defects in teeth, since the enamel-forming cells are unable to withdraw from the blood the materials required for the formation of normal cells. McBeath<sup>38</sup> and Erpf<sup>39</sup> found a seasonal variation in the incidence of dental caries, the highest incidence of new cavities occurred in late winter and spring, when the amount of sunshine was the lowest. It is thus apparent that the lack of sunshine may be to blame for a lowered production of vitamin D in the bodies of the children as a result of the reduced amount of ultraviolet light. This decrease was manifested in part by the increased amount of dental caries observed during the period of low vitamin D production.

The eating of sugar and candy has been believed by many authors to cause dental decay. Bunting and his associates<sup>41</sup> were able to demonstrate that children classed as immune to caries who were allowed to eat about 3 pounds of candy a week soon became susceptible to dental decay. Thus, sugar seems to be a greater menace to the teeth than are starchy foods. This observation has been verified by studying the diets of starch-eating primitives, who usually have relatively small amounts of dental decay.

In conclusion, it may be said that if a person has an optimal diet during the developmental period of the teeth, they will be free from defects such as pits, fissures and hypoplastic enamel. Subsistence throughout life on a strictly carnivorous diet prevents caries. The presence of considerable carbohydrate, especially sugar, in the diet is likely to predispose to dental decay. The elimination of sugar from the diet, with the substitution of starch, affords a less favorable oral medium for the development of acid-forming organisms and so protects the teeth against acid decomposition. Vigorous chewing of raw fruits or raw vegetables, which also act as detergents, tends to prevent dental caries.

### Mouth Bacteria

Bibby<sup>3</sup> summarized as follows the reasons why bacteria are believed to be of fundamental importance in causing dental caries. Tooth destruction progresses from the outside of the teeth inward, the sites at which caries occur are the places at which foods accumulate, an association has been shown to exist between the acidogenic properties—carbohydrate content—of diets and their effects in producing caries, as yet acids are the only chemical and biologic agents that are known to have the power of destroying dental enamel and bringing about decalcification of dentin, and lastly, bacteria are the only agents existing in the mouth that are known to have the power of producing acid from foodstuffs.

Accumulated evidence indicates that acid is definitely concerned in tooth decay. Enright et al.<sup>40</sup> demonstrated that cavities like those of caries can be produced by the action of acids. Bunting<sup>41</sup> and

Bibby<sup>42</sup> were able to produce similar cavities by bacteria grown in the presence of carbohydrates. Oslick<sup>43</sup> found that the acidity of dental mucous plaques is increased when fermentable carbohydrates represent. Deakins<sup>44</sup> demonstrated that the chemical changes that occur during the formation of caries correspond to those caused by the action of acid. Miller<sup>45</sup> and Kanthak<sup>46</sup> found organic acids in carious dentin. Finally, Miller<sup>47</sup> and Hodge and Inn<sup>48</sup> were able to demonstrate that certain agents that prevent acid formation from carbohydrates prevent dental caries in animals, and Dean, Jay, Arnold, McClure and Elvoie<sup>49</sup> and Day<sup>50</sup> were able to demonstrate the same fact for man.

Culture studies by various investigators have led them to postulate a causative relation between dental caries and certain bacteria, on this basis lactobacilli, streptococci, fusiform organisms, species of Cladothrix and Leptothrix and anaerobic bacteria have been named as etiologic agents of dental caries. Bunting et al.<sup>51</sup> have reported an extensive study of the association between increases in the number of lactobacilli and dental caries, lactobacilli were shown to decrease when cavities were filled or carious teeth were extracted. As yet no specific bacteria have been positively proved to be the prime cause of dental decay. It may therefore be concluded that several types of bacteria are associated with dental decay and that any organism that produces acid in the mouth is a potential cause of decalcification. Experiments conducted by Bibby,<sup>42</sup> however, indicate that lactobacilli are present in a relatively small number and may be caused by conditions brought about through dental caries, whereas streptococci are present in relatively large numbers, grow more rapidly, are active in bringing about chemical changes and may in effect be the bacterial flora chiefly responsible for dental decay.

#### Cost of Dental Care

It is readily understood that the repair of the constant damage produced by dental caries is costing the Nation large sums of money annually. These costs are for repairing teeth that develop cavities, extracting those that are beyond repair and providing replacements for lost teeth that are required for the mastication of food. Detailed information regarding the prevalence of dental defects among the entire adult population of the United States is limited. Surgeon General Parran<sup>2</sup> in a statement before a congressional committee in a hearing on a bill to provide greater facilities for dental care gave an estimate, prepared by one of the dentists of the United States Public Health Service, of the accumulated dental needs of the population. In the same statement he gave a list of the average charges for various items in dental care. On the basis of these figures Table 2 has been prepared. It shows that it would cost over \$4,000,000,000 to repair the damage done by dental caries and pyorrhea to

the teeth of the American population, the share of Massachusetts being nearly \$134,000,000. This amount represents a per capita cost of \$31.00. Once the teeth were put in good repair, the constant inroads of dental caries would produce additional damage, the repair of which would cost further sums.

It is obvious that there are not sufficient dentists and dental assistants in the Nation to take care of this accumulated volume of dental work. The best

TABLE 2 Dental Needs for the United States

ITEMS	NO NEEDED	AVERAGE COST PER ITEM	TOTAL COST	COST FOR MASSACHUSETTS
Extractions	238,500,000	\$2.00	\$477,000,000	\$15,700,000
Fillings	632,000,000	3.50	2,212,000,000	72,600,000
Prophylaxes	125,000,000	2.00	250,000,000	8,200,000
Dental treatments	20,000,000	2.00	40,000,000	1,300,000
Crowns and bridges	39,500,000	15.00	592,500,000	19,500,000
Partial dentures	20,000,000	25.00	500,000,000	16,500,000
Totals			\$4,071,500,000	\$133,800,000

study available on the total annual expenditures for dental care in the United States is that made in 1929 by Leven and Beck,<sup>52</sup> who estimated the gross annual income of dentists as \$446,000,000, about one ninth of the \$4,000,000,000 mentioned above. In other words, it would take the men now trained in dentistry approximately nine years to care for the accumulated needs of the American people.

On the premise that the destruction of teeth by dental caries and pyorrhea will continue at the present rate, Dollar<sup>53</sup> has estimated the annual cost of maintaining the teeth of this population in good repair as \$1,300,000,000. This is about three times as much as is being expended for dental service at the present time. The figure for Massachusetts would be almost \$43,000,000.

It is self-evident that if the inhabitants of this country are to have good teeth, either there must be provided a sufficient number of dentists and dental assistants who are adequately paid or ways must be found for halting the inroads of dental caries and pyorrhea. This is the reason why those interested in dental health<sup>54, 55</sup> are looking so hopefully toward the use of fluorine and of other agents that give promise of reducing the annual damage by diseases of the teeth and gums. For this reason also, health departments should have a part in carrying on studies that will uncover other measures for stopping this annual drain on the health, energy and financial resources of the Nation.

(To be concluded)

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

## CASE 32231

### PRESENTATION OF CASE

A fifty-one-year-old housewife entered the hospital because of burning, tingling and pain in the fingers

The patient was allegedly well until six months before admission, when she began having a dull aching in her fingertips followed several weeks later by severe burning and tingling. At first these symptoms came in paroxysms, but they gradually became constant, lasting day and night and spreading to involve the entire hands. There was no definite story of weakness, but the paresthesias limited the use of her hands to such an extent that they became stiff and she was finally unable to feed herself. She saw her physician, who diagnosed anemia and treated her with liver and iron injections, as well as with many vitamin preparations. During this medication she developed anorexia, and three weeks before entry she began to vomit everything she ate. Concomitantly, she noticed swelling of the ankles, mild pain in the calves and some difficulty in walking. The pains in her arms were somewhat less when she sat on the edge of her bed, and she spent much time in that position.

In the past her health had been good except for an attack of gout in the great toe thirty years previously and a tubal pregnancy followed by a salpingo-oophorectomy seventeen years before entry. She had had two normal deliveries. The menopause had occurred four and a half years before entry.

Physical examination revealed a well developed but rather obese pale woman in no acute distress. The mucous membranes were pale. The skin was dry. The tongue had smooth edges, but it was not red and there was no cheilosis. An inconstant Grade I systolic murmur was heard over the apex. The lungs were clear. The abdomen was obese. The arms showed moderate weakness of all motions and marked weakness of the hands. There was considerable limitation of passive motion of the fingers, elbows and shoulders. The wrists and shoulders were somewhat tender. There was hyperesthesia to pain, and vibration and position senses were normal. The

thenar eminences were flattened. The legs showed no limitation of motion and no paresthesias. Vibration and position senses were moderately decreased. There was moderate calf tenderness.

The temperature, pulse and respirations were normal. The blood pressure was 150 systolic, 85 diastolic.

Examination of the blood showed a red-cell count of 3,100,000, with a hemoglobin of 9 gm. The smear was reported as normocytic and normochromic. The white-cell count was 23,500, with 90 per cent neutrophils and 9 per cent lymphocytes. The non-protein nitrogen was 92 mg per 100 cc, and the protein 5.7 gm. The Hinton and Wassermann tests were negative. The urine showed many white cells in clumps but no albumin or casts. The specific gravity was 1.010. Culture revealed a moderate number of colon bacilli.

X-ray films of the chest and a gastrointestinal series were reported normal.

Lumbar puncture showed an initial pressure equivalent to 170 mm of water and a final pressure of 140 mm, with free dynamics. There were no cells, and the ammonium sulfate ring-test was negative. The total protein was 21 mg per 100 cc. Gold-sol and Wassermann tests were negative.

The patient was extremely unco-operative and resisted efforts to mobilize her. She complained constantly of the pains in her joints and muscles. She was oriented during the day, but at night she had severe delirium with nightmares and hallucinations despite sodium amytal sedation.

On the fifth hospital day she was transfused with 500 cc of whole blood. On the ninth hospital day the white-cell count reached 30,000, with 82 per cent neutrophils and 18 per cent lymphocytes, some of which appeared atypical. Further urine studies showed a + test for albumin, failure to concentrate to a specific gravity of more than 1.014, and less than 5 per cent excretion of phenolsulfonephthalein at the end of two hours. The patient gradually became oliguric and passed into coma. On the nineteenth hospital day the nonprotein nitrogen reached 140 mg per 100 cc and the carbon dioxide 7.5 milliequiv per liter. She died on the twentieth hospital day.

### DIFFERENTIAL DIAGNOSIS

DR. MARIAN W. ROPES: I am sure that the one safe statement is that I am unable to make a diagnosis that will completely fit this picture. There are a few obvious facts: the patient was in uremia when she came to the hospital, she had an infection of the urinary tract, she had anemia, leukocytosis and neurologic and skeletal symptoms, and she died of renal failure. Several diagnoses are suggested by these symptoms, and the problem is to pick one that will correlate all the findings.

In any patient with renal disease, anemia and skeletal pain one thinks of multiple myeloma. There is no more than that to support this diagnosis, how-

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in the urine. The strongest point in favor of pyelonephritis is the presence of urinary-tract infection at the time of admission. Unfortunately, we know nothing about the duration of the infection. Apparently there were no symptoms associated with the genitourinary tract before her present illness. In fact the only renal disease that I was able to think of that gives as few changes in the urine is amyloid disease, which frequently shows only albumin in the urine. I have never happened to hear of or see a patient with so little albumin in the urine at the time of death from amyloid disease of the kidney. That would not rule it out, however. We have seen patients who died of amyloid disease who had had nothing except albumin in the urine throughout the course of the disease.

It is of interest to compare this case with one reported by Lengh\* in 1937. The patient was a forty-seven-year-old woman who six months before entry had pain in the joints, paresthesias and anemia and at the time of admission had some albumin in the urine. She died soon after her hospital admission and at autopsy was found to have pyelonephritis, with stones and atypical amyloid disease, masses of amyloid being present in the joint tissues. It also involved the tongue and many vessel walls—a few in the liver, spleen and heart and many in the kidneys. The explanation that Lengh gave in this case was that it was amyloid disease secondary to severe infection—a pyelonephritis of years' duration. The involvement of tissues in that case is much like that reported in atypical amyloid disease or so-called "paramyloidosis," in which the liver and spleen are not involved but amyloid is present in muscles, joints, bones, the tongue and thyroid gland and the vessel walls, often in the kidneys. Interestingly enough this particular atypical form is usually not secondary to any known cause. Infection is generally not found. In the secondary type of amyloidosis in which the liver and spleen are often involved the cause of the amyloid is usually an infection.

In trying to put together the diseases suggested by the neurologic and skeletal symptoms and the diseases suggested by the kidney disease, I find it difficult to offer an adequate explanation of the entire picture. I shall say first that she had an infection of the urinary tract. It is obvious that she had uremia, which was probably due, I shall say, to amyloid disease. Whether or not the amyloid disease was secondary either to one of the group of connective-tissue diseases that I have discussed or to the renal infection, or whether it represented the so-called "atypical amyloid," which would explain all the other symptoms, I cannot tell. The possibility of explaining it on the basis of atypical amyloidosis is intriguing.

DR BERNARD JACOBSON In addition to amyloid disease, would you not consider Bence-Jones proteinuria as a possibility?

DR ROPES I mentioned Bence-Jones proteinuria as a cause of the renal disease, but in the absence of other evidence I ruled it out. The renal evidence is satisfactory, but I cannot explain the rest of the picture on that basis.

DR CHESTER M JONES We did not know what the patient had. We thought of many of the things that Dr Ropes has outlined. As a matter of fact, chronic renal disease was not too seriously considered for several days because the first and second specimens of urine had no albumin, the third and fourth specimens gave only a + test for albumin and contained white cells but no other formed elements. My feeling was that she had chronic glomerulonephritis. She had a fixation of gravity at 1010, and practically no dye was excreted in the phenolsulfonephthalein test. The other findings were those of a person who had prolonged anorexia and vomiting, with malnutrition and deficiency disease, and possibly a thiamin lack, with a peripheral neuritis, for which she was also treated. Incidentally she had been treated with liver by her own doctor without any apparent improvement. Dermatomyositis was considered, but there was no evidence that that existed.

#### CLINICAL DIAGNOSES

Chronic glomerulonephritis  
Uremia  
Peripheral neuritis

#### DR ROPES'S DIAGNOSES

Chronic pyelonephritis  
Uremia  
Amyloid disease (? atypical form)

#### ANATOMICAL DIAGNOSES

Diffuse plasma-cell myeloma  
Lower nephron nephrosis (Bence-Jones proteinuria type)  
Atypical or "primary" amyloid disease, involving muscles, joints, heart and blood vessels  
Chronic pyelonephritis, minimal

#### PATHOLOGICAL DISCUSSION

DR MALLORY Obviously this was a very difficult case for diagnosis, and Dr Ropes has come astoundingly close. Everything can be explained on the basis of one condition and its recognized complications. The patient did have extensive amyloid disease with the distribution of the so-called "atypical" or "primary" type, with marked involvement of the muscles, joints, heart and blood vessels. The liver, spleen and kidneys were entirely free from the disease. The kidneys showed massive plugging of all the lower nephrons with hyaline casts and severe interstitial nephritis, with a few foci of pyelonephritis, which were relatively unimportant.

\*Lengh, F. Zur Kenntnis der Amyloidablagerung in den Gelenken. *Deutsch. allg. Path. u. path. Anat.* 69:1-5, 1937.

ever, unless we assume the unlikely possibility that the atypical lymphocytes might have been plasma cells. Such a diagnosis would not explain the degree of muscle involvement or paresthesias. Similarly, with paresthesias, anemia and smooth tongue edges, one thinks of pernicious anemia, but we are told that on at least one examination the blood was normocytic and normochromic. She had had some treatment that might have modified the picture, but there was no evidence in the blood examination that she had pernicious anemia. Furthermore, the neurologic examination was essentially normal. The vibration and position senses were normal, except for slight reduction in the legs. Also this diagnosis would not explain the renal involvement or the degree of muscle involvement. The neurologic findings suggest polyneuritis, but the course is against such a diagnosis. The relatively normal neurologic examination is against it, and particularly against it is the normal spinal fluid. If such a diagnosis were to be made it would be separate from the renal involvement. I think we can rule that diagnosis out. One can also rule out muscular dystrophy. In fact the degree of muscle change is so slight that I doubt that such a diagnosis could even be considered. There was weakness but relatively little, — more pain than weakness, — and the paresthesias were out of proportion for such a diagnosis. There is minimal evidence to suggest leukemia or lymphoma, and I think that they can be ruled out.

In any constitutional disease that has joint and muscle involvement, paresthesias and anemia, we have to think of connective-tissue diseases, such as rheumatoid arthritis, disseminated lupus erythematosus, periarteritis nodosa, dermatomyositis and scleroderma. The last can be easily ruled out because there was no skin involvement. Dermatomyositis is possible because of the degree of involvement of the muscles. Absence of real inflammation of the muscles and absence of weakness in the trunk or pharyngeal muscles would be unlikely in a severe case of dermatomyositis. Again, this would not explain the renal involvement. The other three conditions cannot be ruled out, although I find little evidence for any of them. The joint and muscle symptoms are consistent with rheumatoid arthritis. Unfortunately we have no x-ray films of the joints, and I judge that the other films were negative.

DR TRACY B. MALLORY: There is one shoulder joint showing in this chest film.

DR ROPES: In it there is nothing except the suggestion of some loss of calcium from the bones. There is no definite soft-tissue involvement of which I can be sure.

There is a story of a joint attack in the past that was called "gout." I think that this is of no significance so far as the present illness goes. Indeed, I doubt that she had gout. It is extremely rare in women, and an attack of acute arthritis involving

the great toe is often called gout without further evidence. My feeling is that she had another type of arthritis in the great toe. We cannot rule it out, but I think that she did not have gout with a progressive arteriosclerosis causing the renal failure.

If rheumatoid arthritis is to be considered as the cause of the recent condition, it would not explain the renal involvement unless the patient had amyloidosis. The development of amyloid in rheumatoid arthritis within a six-month period is unusual. It occurs after various changes in the blood have taken place, such as an increased globulin, but in our experience it does not occur until after at least six months and usually after a year of disease. The evidence we have is that her illness did not start until six months before admission. I doubt that she had amyloid due to rheumatoid arthritis.

Joint and muscle symptoms can occur in disseminated lupus, but here, as in rheumatoid arthritis, one would not expect such severe paresthesias or marked muscle changes. The diagnosis of lupus would, of course, explain the renal involvement and renal failure as the cause of death, but it is impossible to make the diagnosis of disseminated lupus in the absence of involvement of the skin and serous membranes. Furthermore, a leukocytosis of this degree would be extremely unusual, if not unknown, in lupus without obvious infection. In fact the majority of cases of disseminated lupus, even with infection, do not elevate the neutrophil count to this level.

Periarteritis nodosa is perhaps more difficult to rule out despite the fact that there is again no definite evidence for it. The degree of paresthesia is greater than one ordinarily sees with periarteritis nodosa, and the degree of muscle weakness and muscle change is much greater than one ordinarily sees. If the renal involvement were due to periarteritis nodosa one would expect more abnormalities in the urine than a + test for albumin with, on one occasion, many white cells. I am assuming that the other urinary specimens were essentially negative. So the group of diseases suggested by the skeletal and neurologic symptoms do not explain the entire picture.

I might turn to the renal involvement and consider the likely causes of renal failure that lead to death. There are few conditions that show an essentially negative urine at the time of renal failure. From the whole picture — the age, the lack of arteriosclerosis elsewhere and the relatively negative urinary findings — it is unlikely that the patient had nephritis on the basis of arteriosclerotic changes. Chronic glomerulonephritis cannot be ruled out. She went slowly into uremia, and at that time she was known to have an infection of the urinary tract, but again, one would surely expect more changes in the urine. Similarly pyelonephritis cannot be ruled out, although one would expect more changes

present a tumor of this size. It is usually a small tumor, whose only symptom is intermittent obstruction, and that does not fit the picture in this case, because this is a large tumor with extensive ulceration of the mucous membrane as shown by x-ray and by the occult blood in the stools.

The time is nearly up and I shall not discuss this any further. I shall say that the most probable

he would have been able to tell more accurately, but I should say that this was a lymphoblastoma or lymphosarcoma of the jejunum.

DR TRACY B MALLORY: Dr Simeone, will you give the operative findings?

DR F SIMEONE: At operation this patient had a large mass about 9 or 10 cm in diameter, which was stony hard to palpation and, on the surface,



FIGURE 1 X-Ray Film Showing Displacement of the Proximal Transverse Colon by a Midabdominal Mass

diagnosis is tumor of the small bowel, not of the carcinomatous type, which would cause constriction and would be small. Because of its size the tumor had probably grown both within and outside the bowel, invading the mesentery. Myoma, fibroma and lipoma are possibilities but the more frequent variety is lymphoma, perhaps of the Hodgkin's type. We have no further evidence of that, however. Perhaps if an expert hematologist had seen a smear

appeared white. The mass was freely movable in the horizontal plane from right to left and back again, but could not be moved in the vertical plane. It could not be delivered into the wound. The mass had infiltrated the mesentery to a great extent. On tracing it down it was found to extend to the origin of the midcolic artery and for that reason we believed that it was certainly incurable, but we wanted to make every effort to remove the tumor.

One very peculiar and I think probably pathognomonic finding was that there were foreign-body giant cells around the casts within the tubules. I have never seen that except in Bence-Jones proteinuria. I was first shown the kidney in this case, and because of this finding asked to see the bone marrow, which proved to be diffusely invaded with plasma cells. So the primary diagnosis is diffuse plasma-cell myeloma, with Bence-Jones proteinuria, the so-called "myeloma kidney." Amyloid disease is a recognized sequel of myeloma and oddly enough nearly always shows the distribution of so-called "primary" amyloidosis rather than that of the usual secondary type.

DR JACOBSON: What was the serum protein value?

DR JONES: It was 5.7 gm per 100 cc. The service considered doing a bone-marrow biopsy, but the patient was so ill that it was not done.

DR MALLORY: I do not believe that the serum protein value was checked.

DR. ROPES: The low serum protein might be explained by the fact that she had lost albumin in the urine over a long period.

DR JACOBSON: It is interesting that this is one of the few cases autopsied here that has shown atypical amyloid distribution.

DR MALLORY: I can remember only one other

## CASE 32232

### PRESENTATION OF CASE

A fifty-three-year-old shoe cutter entered the hospital because of progressive weakness, and loss of weight.

The patient had been in apparent good health until ten months before entry, when he vomited four times in one night. He went to a local hospital, where x-ray films were taken, but was sent home with some pills. He did not vomit again, but became progressively weaker and lost about 15 pounds. Several weeks before entry he noticed increasing anorexia, constipation, flatulence and a feeling of abdominal fullness. The stools were darker than usual, but not black, and he noticed no blood. He also suffered from sour stomach, which was aggravated when he was lying down.

Physical examination showed a pale, lethargic man, with evidence of recent weight loss. The mouth was edentulous. The heart and lungs were normal. At the level of the umbilicus there was an irregular, hard, freely movable abdominal mass, about 12 cm in diameter, which could readily be shifted to either side of the umbilicus and caused marked local protuberance of the abdomen. Peristaltic sounds were rather high pitched. The liver could not be palpated. Rectal examination was negative except for moderate enlargement of the prostate.

The temperature, pulse and respirations were normal. The blood pressure was 120 systolic, 60 diastolic.

Examination of the blood revealed a hemoglobin of 8 gm. The white-cell count was 8200. The non-protein nitrogen was 31 mg and the total protein 6.8 gm per 100 cc, and the chloride 102 milliequivalents per liter. The prothrombin time was normal. The urine was normal. Repeated stool examinations were guaiac positive.

X-ray examination of the abdomen, including an intravenous pyelogram, showed normal kidneys. There were several diverticula of the urinary bladder, measuring up to 4 by 1.5 cm. A barium enema readily filled the entire colon and terminal ileum, showing them to be normal in form and function. The colon contained some fecal material, particularly in the ascending and proximal transverse portions. On the post-evacuation film the proximal transverse colon was displaced slightly upward by extrinsic pressure from the midabdominal mass, which was shifted upward as compared with its position on the pre-evacuation film (Fig 1). A small intestinal enema revealed an area of ulceration, measuring approximately 6 cm, in the upper jejunum, within the freely movable palpable mass (Fig 2). The bowel was slightly narrowed in the region of the ulceration, but most of the mass lay outside the bowel lumen, pushing aside the remainder of the intestinal loops in this area. Some of these loops seemed to be attached to the tumor mass.

An operation was performed on the ninth hospital day.

### DIFFERENTIAL DIAGNOSIS

DR HORACE K. SOWLES: May we see the x-ray films?

DR RICHARD SCHATZKI: The mass is fairly well visualized in the post-evacuation film, where it displaces the colon (Fig 1). The films of the small intestine again outline the mass that displaces the loops of intestine, but one is seen going straight through the mass, where the ulceration described in the report (Fig 2) is visible. It can be seen even better on the spot films, which also show slight dilatation of the jejunum proximal to the narrow ulcerative region.

DR SOWLES: This patient had symptoms of intestinal obstruction, although he had only one real attack. On admission, he had a low hemoglobin, a history of loss of weight and weakness. One immediately thinks of neoplasm of the right colon, in which the only presenting symptoms are sometimes anemia and loss of weight and weakness. As we go along in the history we find that the colon apparently was normal by barium enema whereas the small bowel showed a definite tumor in the jejunum—a large tumor with ulcerations of the mucous membrane. I think we can rule out carcinoma, which is quite rare in the jejunum, and does not

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## THE MEDICAL CENTER FOR CHILDREN AT THE CHILDREN'S HOSPITAL

THE *Journal* notes with interest the recent announcement of the proposed expansion of the Children's Hospital leading to its transformation into the Medical Center for Children.

During its seventy-seven years of service the Children's Hospital has earned world-wide recognition for the quality of its medical and surgical work, for its research and for its training of medical students, physicians, nurses, physiotherapists and other workers especially interested in the problems of early life. To its wards have been brought young patients from all over New England and indeed from distant places, both in this country and overseas.

Its graduates are active in the practice of their specialties throughout the world.

The increased demands on the resources of the hospital, particularly from the New England area, the obsolescence of many of its buildings, and the opportunity for expansion of existing services and the creation of new units afforded by the constant effort of the staff to improve its work have led to the development of the Medical Center for Children. The heart of the plan, of course, is the Children's Hospital, with new and expanded facilities for the care of all aspects of disease in early life. To bring to older children, whose problems have long been neglected, all the medical, surgical and psychiatric assistance that will be available to younger patients, a new division of the Children's Hospital, a unit for adolescents, will be added. A neurologic institute, embracing the fields of neurology, neurosurgery and psychiatry, a greatly expanded infectious-disease division, with additional provisions for the care of patients with poliomyelitis, a cancer center and a greatly enlarged and completely equipped division of pediatric research form parts of the new plan. To assist in the most economical and efficient manner the doctors of New England who deal with young patients, a series of diagnostic clinics will be established. Similar facilities will be available in the several laboratory divisions that are designed to act as centers for consultation in chemical, clinicopathological, bacteriological and pathological aspects of pediatrics. In the field of preventive medicine, a health unit founded to bring to the problems of the healthy child from birth through adolescence all the specialized talent available in such a medical center should do much to raise the level of mental and physical health in New England and, in the course of time, to reduce the burden of disease.

To enable the Medical Center for Children to render the greatest possible service to the New England community, plans are now under way for appropriate affiliation with physicians and pediatric wards of general hospitals throughout this area, in extension of the unique relation that has existed for so long between the doctors in this region and the Children's Hospital. This affiliation, it is planned, will include not only arrangements for the

because one of the symptoms was the big mass in the abdomen, which disturbed the patient. The resection carried us into the pancreas and to the mid-colic artery. We thought it was unwise to go farther, in spite of the fact that tumor tissue appeared to

#### DR. SOWLES'S DIAGNOSIS

Lymphosarcoma of jejunum

#### ANATOMICAL DIAGNOSIS

Adenocarcinoma of jejunum



FIGURE 2 X-Ray Film of the Upper Jejunum  
The arrow points to the ulceration in the jejunum

extend beyond that point. Because of the amount of mesentery that had to be removed it was necessary to resect the entire jejunum and to mobilize the third portion of the duodenum from beneath the ligament of Treitz. An end-to-end anastomosis was done between the duodenum and the ileum.

#### CLINICAL DIAGNOSIS

Carcinoma of jejunum

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: This clinic today is a good example of what poor judgment it would sometimes be to make the correct diagnosis. The last case\* should have been a benign tumor but proved to be a malignant one. This case showed a typical ulcerative carcinoma, which had extended very deeply into the mesentery and had also become adherent to and invaded an adjacent loop of small bowel.

\*Case records of the Massachusetts General Hospital (Case 32211).  
*New Eng. J. Med.* 234:701-703, 1946.



clinical use are the sodium and calcium salts of penicillin G

These findings alone are of considerable general interest. Other features of the chemistry of penicillin, more important perhaps to the chemist and pharmacologist than to the clinician, are also published for the first time. According to the information thus far revealed it seems highly doubtful that synthetic penicillin will be forthcoming in the immediate future. Even should such synthesis be accomplished in the laboratory, it does not follow that the large-scale production of synthetic penicillin would be economically feasible. It is well known that the commercial manufacture of such simple substances as acetic and citric acids and various simple alcohols is best accomplished by fermentation methods, and the same may prove to be the case with penicillin

MASSACHUSETTS MEDICAL SOCIETY

DEATH

LANDESMAN — Henry M Landesman, M D, of Boston, died May 22. He was in his sixty-second year. Dr Landesman received his degree from the College of Physicians and Surgeons, Boston, in 1917. He was a fellow of the American Medical Association and a member of the Massachusetts Association of Examining Physicians and the South End Medical Club. His widow and a daughter survive.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1946

RÉSUMÉ			
DISEASES	APRIL 1946	APRIL 1945	SEVEN-YEAR MEDIAN
Anterior poliomyelitis	2	2	1
Chancroid	2	2	1
Chicken pox	2	2	1
Diphtheria	1751	963	1181
Dog bite	16	25	13
Dysentery bacillary	1251	1286	945
German measles	10	0	2
Gonorrhea	1150	195	398
Granuloma inguinale	453	463	355
Lymphogranuloma venereum	0	0	*
Malaria	1	4	*
Measles	35	124	3
Meningitis meningococcal	8612	732	4012
Meningitis, Pfeiffer-bacillus	14	16	16
Meningitis, pneumococcal	3	2	2
Meningitis, staphylococcal	5	7	6†
Meningitis, streptococcal	0	0	0†
Meningitis, other forms	0	0	1†
Meningitis undetermined	2	2	2†
Mumps	4	5	9†
Parasomia, lobar	924	2431	1482
Salmonella infections	128	322	360
Scarlet fever	3	6	5
Syphilis	824	1422	1422
Tuberculous pulmonary	454	342	425
Tuberculous other forms	245	206	224
Typhoid fever	12	7	18
Undulant fever	3	2	3
Whooping cough	9	2	3
	477	568	625

\*Made reportable December 1943  
†Four-year average.

COMMENT

Diseases reported at figures above the seven-year median included chicken pox, bacillary dysentery, German measles, pulmonary tuberculosis and undulant fever. Measles was also reported above the seven-year median, reaching a peak since 1906 that is second only to the record year of 1934. Reported at figures below the seven-year median were mumps, scarlet fever and whooping cough. Record low figures were reported for lobar pneumonia. The first case of animal rabies since February, 1944, was reported from the central part of the Commonwealth. The animal was a recent arrival from a nearby state.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

Anterior poliomyelitis was reported from Deerfield, 1, Springfield, 1, total, 2. Diphtheria was reported from Andover, 1, Arlington, 1, Boston, 5, Chelsea, 1, Cushing General Hospital, 1, Falmouth, 2, Haverhill, 1, Malden, 1, Millville, 1, Taunton, 1, West Newbury, 1, total, 16. Dysentery, bacillary, was reported from Belmont, 1, Boston, 2, Cambridge, 3, Lowell, 1, Peabody, 1, Wrentham (State School), 2, total, 10. Encephalitis was reported from Chatham, 1, total, 1. Malaria was reported from Amherst, 1, Boston, 8, Cambridge, 1, Chelsea, 1, Fall River, 2, Gardner, 1, Haverhill, 1, Hingham, 1, Lawrence, 1, Lynn, 1, Nantucket, 1, New Bedford, 1, Peabody, 1, Salem, 1, Southbridge, 1, Stoughton, 1, Waltham Regional Hospital, 2, Warren, 2, West Springfield, 1, Woburn, 1, Worcester, 5, total, 35. Meningitis, meningococcal, was reported from Boston, 4, Fall River, 1, Lee, 1, Ludlow, 1, Malden, 1, Medford, 1, Millbury, 1, Quincy, 1, Salem, 1, Wayland, 1, Worcester, 1, total, 14. Meningitis, Pfeiffer-bacillus, was reported from Cohasset, 1, Haverhill, 1, Saugus, 1, total, 3. Meningitis, pneumococcal, was reported from Abington, 1, Brockton, 1, Gloucester, 1, Natick, 1, Pittsfield, 1, total, 5. Meningitis, other forms, was reported from Boston, 2, total, 2. Meningitis, undetermined, was reported from Dalton, 1, Framingham, 1, North Adams, 1, Springfield, 1, total, 4. Salmonella infections were reported from Malden, 1, Northampton, 1, Springfield, 1, total, 3. Septic sore throat was reported from Arlington, 1, Belmont, 1, Boston, 4, Everett, 1, Greenfield, 1, Haverhill, 1, Newton, 2, Norfolk, 1, Westford, 2, Weston, 1, total, 15. Tetanus was reported from Pittsfield, 1, total, 1. Trichinosis was reported from Adams, 1, Boston, 4, total, 5. Typhoid fever was reported from Boston, 1, Chicopee, 1, Waltham, 1, total, 3. Undulant fever was reported from Belmont, 1, Boston, 1, Deerfield, 1, North Andover, 1, Oxford, 1, Quincy, 1, Southbridge, 1, Tewksbury, 1, Yarmouth, 1, total, 9.

REPORT OF MEETING

NEW ENGLAND ROENTGEN RAY SOCIETY

The New England Roentgen Ray Society held its last meeting of the season on Friday, May 17, 1946. The following officers were elected for the ensuing year: president, Dr Samuel A. Robins, vice-president, Dr Stanley A. Wilson, secretary, Dr George W. Holmes. The second George W. Holmes Annual Lecture was delivered by Dr Arthur C. Christie, of Washington, D. C. Dr Christie's subject was "The First Fifty Years of Radiology. The elements which have contributed to its growth as a great medical specialty." Dr George W. Holmes and Dr Christie were presented with the Society's silver colonial pitcher, which is emblematic of the occasion. Dr Holmes received congratulatory telegrams from his former students in various parts of the country.

care of specialized medical and surgical cases but also provision for the training and postgraduate education of practicing physicians, interns, nurses and other workers with special interest in pediatrics

The essence of the Medical Center for Children is the gathering under one roof, for a combined attack on the manifold problems of health and disease of the infant, the child and the adolescent, doctors and medical workers whose major interests concern these age groups, with the aid of all the technics and specialized knowledge available in the medical world today

The long history of distinguished contributions of the Children's Hospital to the various medical, surgical and laboratory aspects of disease of infancy and childhood is a guarantee of the success of this ambitious but wholly logical and practical plan. The *Journal* extends its best wishes to the Board of Trustees and to the Medical Staff of the Children's Hospital in their great undertaking

## CHEMISTRY OF PENICILLIN

IN SHARP contrast to the many useful functions performed during the war by Government-supported research, there was at least one undesirable feature of that program, namely, the withholding of newly acquired information. The chief purpose of that secrecy—to keep from the enemy all information that may give him aid and comfort—is quite understandable. On the other hand, this policy has often served to channel information within a relatively small group of workers and away from others, perhaps of equal competence, who might have put that information to good use. The disadvantages and dangers of this sort of secrecy and the importance of the freedom to publish the results of scientific research are well recognized, and a vigorous attempt to preserve that freedom in any program of federally supported research is being made by a number of leading scientists

Now that the war is over, there is still a good deal of scientific information that is being considered as "secret" or "classified" and is not yet published or otherwise freely available. Although there may be some justification for this attitude in matters of

immediate national defense, such as those involved in the methods of manufacturing atomic bombs, many facts concerned with health are also included. Some of the latter information is gradually coming to light. Because of the vast amount of research and the colossal number of papers that are undoubtedly available for publication on certain subjects, the Committee on Medical Research and other similar bodies have wisely adopted the policy of summarizing the results of research in certain vital fields in advance of the publication of the detailed results

One of the first of these summaries concerns the chemistry of penicillin.\* Many of the most outstanding among the research laboratories in the United States and Great Britain participated in the program. Although the exact structural formula of penicillin is still undetermined, and its synthesis has not yet been accomplished, some of the most significant aspects of its chemistry have been determined beyond reasonable doubt.

Previously published reports had indicated that several forms of penicillin exist, each of which may be derived from cultures of the same strain of *Penicillium*. The usual form is penicillin G, which is the chief active ingredient of the commercial preparations now available. In addition, penicillin X has been described, and limited experimental and clinical studies of its use have been made in this country. Another form, penicillin F, has also been recognized in this country and in Great Britain. According to the joint report by the Office of Scientific Research and Development and by the Medical Research Committee of Great Britain, the forms of penicillin known as F, G and X in this country and as I, II and III, respectively, in Great Britain, as well as a new form, K-penicillin, all have the empirical formula  $C_{14}H_{18}O_4SN_2R$ . The differences depend on the structure of R. In penicillins G and X, for example, the structures of R are quite closely related, being benzyl in the former and parahydroxybenzyl in the latter. Each different form can, of course, be made into various metallic salts or esters. The varieties of penicillin in general

\*Committee on Medical Research, O. S. R. D., Washington and the Medical Research Council, London. *Chemistry of penicillin*. Science 102: 627-629, 1945.

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## NUTRITION AND THE WAR\*

JOHN B. YOUMAN, M.D.†

NASHVILLE, TENNESSEE

IT IS a distinct honor to be invited to give the Shattuck Lecture, with its long list of distinguished former lecturers and its tradition of excellence of the addresses. I therefore appreciate greatly this honor that has come to me and the opportunity to address the Massachusetts Medical Society on this occasion.

So far as the practice of medicine is concerned, the title of my lecture is somewhat of a misnomer, because the direct contribution of the war to clinical nutrition was not very great. Actual nutritional-deficiency disease was not common in the troops. Most of the actual work in nutrition was in the field of preventive medicine and was not concerned with nutritional disease in the individual patient. Even among prisoners of war and civilian populations, study and observation added little to our knowledge of the severer forms of these diseases. There were, as we shall see, examples of some unusual manifestations of deficiencies. The absence of certain anticipated deficiencies was noteworthy. In Europe particularly the preponderance of caloric and protein deficiency and the rarity of vitamin deficiencies in the civilian populations were striking. But aside from these observations little that is new was obtained from direct observation. The war did, however, intensify interest and speed up research in nutrition. As a result so much has been done that the end of hostilities provides a useful point at which to pause, survey what has been done and consider the place of some of this new knowledge of nutrition in the practice of medicine.

\* \* \*

There are many aspects of nutrition, but those with which the physician is primarily interested are the prevention of nutritional-deficiency disease and its diagnosis and treatment. Ordinarily the physician's interest in the general prevention of nutritional-deficiency disease is rather academic un-

less he happens to be a public-health officer. The private practitioner does have, however, a very real personal interest in this aspect of nutrition, and if he is alert he will maintain a general acquaintance in this field. It is from the general population that his patients are drawn, and the background of nutrition of that population may influence very considerably the nature of the illnesses of his patients, their reaction to disease and their response to his treatment. To some extent this interest, indeed this self-interest, has been appreciated by pediatricians and by a few other physicians, but in general it has not received the attention it deserves. In contrast to general prevention, the prevention of nutritional-deficiency disease in individual patients is of much greater immediate importance to the practicing physician — a problem with which he must deal every day and in some degree or other with almost every patient.

Existing nutritional-deficiency disease is encountered by the doctor in two forms. One is an idiopathic or primary disease caused by a dietary inadequacy, often the result of socioeconomic factors over which the patient may or may not have some control. The other is a conditioned disease in which the deficiency is dependent on some other illness that causes a nutritional deficiency or permits it to develop. The illnesses or abnormalities that cause or induce the deficiency are of the most varied kinds, ranging from severe organic gastrointestinal disease to mild psychoneurosis. This is the kind of nutritional deficiency disease that will be encountered oftenest by the practicing physician and is of the greatest immediate importance to him. It is also the kind that he should be most alert and active to prevent, the more so because such deficiency disease may be the direct result of things he does or fails to do, things directly subject to his control. Often they are relatively simple things, and often failure to control them has a very significant effect on the patient.

There are certain differences between the idiopathic and conditioned type of disease in relation to prevention and treatment. Idiopathic deficiencies ordinarily exist before the patient goes to the doctor. Either they are the disease for which the

\*The Shattuck Lecture, delivered at the annual meeting of the Massachusetts Medical Society, Boston, May 22, 1946.  
†From the Department of Medicine, Vanderbilt University School of Medicine.

†Professor of Medicine, Vanderbilt University School of Medicine, Director, Postgraduate Training for Veterans, visiting physician to Vanderbilt University Hospital.

## BOOK REVIEWS

*Medical Gynecology* By James C Janney, M D 8°, cloth, 389 pp, with 97 illustrations Philadelphia W B Saunders Company, 1945 \$5 00

There have been those who say, "There is no such thing as medical gynecology." It is therefore all the more gratifying that an author of Dr Janney's distinction should devote his new volume to medical office gynecology. It has developed largely from his experience in clinical teaching for the past quarter century, and aims to aid the student in correlating his didactic lectures with his experience in the gynecologic clinic and to provide refresher material for the general practitioner. It follows the standard pattern of other texts — history and examination, symptoms, physical findings, laboratory tests and special examinations, and gynecologic treatments of a medical nature. There are chapters dealing with certain controversial subjects, such as abortion, contraception, illegitimacy and sterilization. Finally, there is an admirable brief section on the alternatives of radiation or surgery in the treatment of gynecologic malignant tumors and of intractable uterine hemorrhage of nonmalignant origin. The book is illustrated with well-chosen cuts and has a classified select bibliography of forty-one titles.

*Trauma in Internal Diseases With consideration of experimental pathology and medicolegal aspects* By Rudolf A Stern, M D With a foreword by Francis C Wood, M D 8°, cloth, 575 pp New York Grune and Stratton, 1945 \$6 75

It is a generally accepted principle of modern society that the workman injured through no fault of his own during the performance of his labors is entitled to compensation. The application of this principle is easy when the trauma is obvious, as, for example, when a fracture is sustained, but can be extremely difficult in the so-called "internal diseases." The wisdom of Solomon often could not decide the degree of aggravation of a duodenal ulcer resulting from employment in a certain occupation. In such cases it is the duty of the physician to advise and enlighten the court.

Those members of the profession who find themselves even occasionally on the witness stand will find this book invaluable. The author has thoroughly reviewed diseases of the heart, lungs, kidneys, gastrointestinal tract, endocrine glands and blood with regard to the role of trauma in etiology or aggravation. Some two thousand sources are listed in the bibliography. Most of these are references to cases that have been decided in court, and it is quite possible that this book will prove to be as useful to the lawyer as to the doctor.

*American Red Cross First Aid Textbook* 12°, paper, 254 pp, with 264 illustrations Philadelphia The Blakiston Company, 1945 Sixty cents

This book has been completely revised, with new illustrations and a rewritten text. It was prepared with great care under the direction of the Committee of Surgery, Division of Medical Sciences, National Research Council. In addition to revision of the chapters on surgery, the medical director of the American Red Cross and his staff fully revised the sections on first aid, water safety and accident prevention. Special chapters were contributed by authorities on injuries to the eye and on snake and other animal bites. The revision is by far the most complete since the book was first published in 1909, and with its splendid illustrations, clear text and adequate index, this volume should become a valuable adjunct to the work of the American Red Cross. In addition, it should appeal to the medical profession and should be in the hands of every first-year medical student. It will find a fitting place in many homes and factories. Every police officer and other public official who has to deal with acute emergencies should be thoroughly familiar with the contents of this book.

*Mass Radiography of the Chest* By Herman E Hilleboe, M D, and Russell H Morgan, M D 12°, cloth, 288 pp, with 93 illustrations Chicago The Year Book Publishers, Incorporated, \$3 50

One of the chief medical dividends of the late war was the vast experience in mass radiography of the chest. This

monograph by two outstanding authorities on that subject is of timely interest and value, as the experiences and technique learned in the induction centers and service installations will undoubtedly be spread to large portions of the civilian population. This manual, as it may properly be called, was prepared for just such use, and it brings together the accumulated information on objectives, planning, equipment and technique, as well as valuable experiences in the procedures necessary to successful surveys of large numbers of people.

The authors lean over backward in the attempt to avoid the charge that such surveys may be interpreted as diagnostic examinations. Many of the common diseases and conditions involving the chest, heart and lungs can be identified quite accurately by the small-film technic. Quite correctly, however, they emphasize throughout the book the fact that their methods are primarily for screening purposes and that detailed clinical studies may be necessary in the positive and doubtful or borderline cases.

The chapter "Roentgen Diagnosis of the Chest" is particularly conservative and might well have been omitted, except that there is no similar primer for the uninitiated, it is to be hoped most sincerely, however, that the untrained will not attempt such an important public-health function.

This manual is of particular value to public-health officers, tuberculosis-control organizations, radiologists and all who are interested in the maximum efficiency and return from public-health expenditures.

## NOTICES

## ANNOUNCEMENTS

Dr Warren D Babb, having returned from military service, has resumed the practice of internal medicine at 40 Chestnut Street, Salem.

Dr Samuel Bolan announces his return from service with the United States Navy and the reopening of his office at 555 High Street, West Medford.

Mr William S Brines took over the position of administrator of the Malden Hospital, Malden, on June 1.

Dr Sidney C Dalrymple, having been released from active duty with the Navy, announces the opening of an office for the practice of medicine at Middle Dyke Farm, Georgetown, Maine.

Drs Channing Frothingham, George P Denny and Victor G Balboni announce the opening of offices for the practice of internal medicine at 101 Bay State Road, Boston.

Dr Luke Gillespie, having been released from military service, has returned to the practice of obstetrics and gynecology at 1180 Beacon Street, Brookline.

Dr Alfred M Glickman announces his return from service with the United States Navy and the reopening of his office at 95 State Street, Springfield, for the practice of surgery.

Dr Elwood O Horne, having recently returned from military service, announces the opening of his office for the practice of general surgery at 36 Pleasant Street, Worcester.

Dr Charles Schlosberg announces his return from military service and the resumption of pediatric practice at 483 Beacon Street, Boston.

Dr Leslie H Van Raalte announces the resumption of private practice limited to gynecology and obstetrics at 15 Lincoln Avenue, Wollaston.

(Notices continued on page xix)

is usually a negative calorie balance, which increases the deficiency of nitrogen (protein)

This phenomenon persists for a variable length of time and exists to a variable degree, depending on factors to be discussed later. If it is severe enough and of long enough duration, the body reserves of protein are exhausted and actual protein deficiency disease develops as I have described. This is responsible for the loss of weight, muscle atrophy, weakness and other effects of such an illness.

This phase, which is often spoken of as the catabolic phase of the reaction to injury or disease, may last for weeks, and is succeeded by an anabolic phase, during which the nitrogen balance becomes positive, nitrogen is retained and protein formed, tissues are restored, and weight is regained. It corresponds to the period of convalescence and recovery.

Besides fractures, this abnormality occurs in a wide variety of other injury and disease — in severe burns, after major surgical operations, especially those in which the peritoneum is opened, with infections such as osteomyelitis and abscesses and with some infectious diseases, such as typhoid fever and meningitis. The cause of this metabolic and nutritional disturbance is not clearly known. There is some evidence that it is linked to the adrenal glands and perhaps to other endocrines. It is a positive, independent reaction not related solely to deficient intake, although intensified by the latter as we shall see. Usually the negative balance continues despite an increase in nitrogen intake, excretion increasing with intake, and in some cases, despite exceedingly large intakes of protein, this negative nitrogen balance cannot be overcome. Because of this and because of its essential nature it has been thought by some to represent a beneficial or protective reaction to injury and disease that should not be overcome.

This specific or essential negative nitrogen balance is exaggerated by a number of other factors that are very important in producing the clinical state of deficiency disease. Following the injury, or with the onset of the disease, there is usually a loss of appetite and a resultant decrease in the intake of food and hence of calories and protein. To this specific loss of appetite there are often added the factors of unappetizing meals, poorly prepared and served, weakness, difficulties brought about by recumbency or by complicated apparatus, nausea and vomiting and the mental changes of illness, all of which interfere with the intake of food. Unfortunately to these must often be added indifference on the part of the doctor and nurse to problems of nutrition, and even misconception and ignorance regarding proper diet and nutrient requirements. The importance of those factors is shown by the results of a survey of food consumption in Canadian military hospitals.<sup>2</sup> This revealed such disparities as a decrease in a diet from about 4000 calories and 156 gm of protein as planned to 2600 calories

and 75 gm of protein as actually served, with a further reduction to 1850 calories and 54 gm of protein actually eaten. Similar studies in one of our own military hospitals revealed high-carbohydrate, low-fat diets for convalescents containing as little as 1400 to 1600 calories and actual intakes as low as 800 calories.<sup>3</sup>

Besides these deficiencies of intake there are other secondary factors affecting nitrogen loss of even greater importance. Although in the primary reaction the nitrogen is lost mainly by urinary excretion, there is often a large added loss in exudates, drainage from wounds and from the surface of burns and even in the sputum and gastric contents and, in those cases with albuminuria, an added loss through the kidneys. Often these losses are tremendous. Thus the specific and primary defect is greatly exaggerated and the nutritional deficiency increased. In diseases not associated with this specific metabolic disorder a nitrogen and protein loss can, of course, occur as the result of simply a dietary deficiency, leading to the same protein-deficiency disease.

The effect of this negative calorie and protein balance depends on its severity and duration and on the nutritional state of the patient. If it is mild and of short duration in a well nourished person, little harm is done. The body has sufficient reserves of protein and body fat to tide him over. To say that in such cases nutritional deficiency disease exists would be incorrect. What has occurred is a metabolic disturbance or abnormality. However, if the reaction is severer and more prolonged, or if it occurs in patients with inadequate reserve of these nutrients, actual deficiency disease does occur. Curiously, if the patient is already much undernourished, the primary, specific negative nitrogen balance does not occur or is of slight degree, as though the body were incapable of responding to an injury or disease in the normal manner. However, reflection will show that under these circumstances the body is already in a state comparable to that reached in the latter stages of the catabolic phase of the reaction, and that nutritional disease already exists.

In addition to the initial reaction, similar, though usually less severe, reactions may occur as the result of complications during the course of the illness. Thus the changing of casts, secondary operations, the opening of abscesses and the occurrence of a secondary or complicating infection or infectious disease may all be accompanied by a return or exaggeration of the nitrogen deficit and of the nutritional-deficiency disease.

The outward manifestation of this deficiency disease is a loss of body weight. At first slight and representing mostly loss of fat, when more severe and continued there is loss of tissue protein, revealed externally by atrophy of muscles. There is, however, also a loss of native protein, from important parenchymatous organs and from the blood plasma.

patient seeks relief, or they are a substratum to which is added whatever other disease the patient may acquire. Conditioned deficiency diseases, on the other hand, are developed subsequent to some other illness. Although often present by the time the doctor first sees the patient, in many cases, especially those associated with acute illness and trauma, they do not occur until after the conditioning disease begins. This gives the doctor opportunity to prevent or minimize them. In conditioned deficiency, then, the opportunity for prevention is greater. In the idiopathic disease, diagnosis and treatment of an existing deficiency is the problem.

At the present time the principal nutritional deficiency diseases that can be diagnosed and are considered to be of clinical significance in man are caused by a lack of the necessary amounts of the following substances: calories, protein, vitamin A, thiamin, niacin, riboflavin, folic acid (*L. casei* factor), ascorbic acid or vitamin C, vitamin K, iron and calcium. There are others, notably those of water and sodium chloride, and perhaps some of the other electrolytes, that we can recognize clinically. Some would add vitamin E, certain of the so-called "trace elements" and perhaps others of the vitamin B complex. But these are not yet well enough established, if indeed they exist, as recognizable clinical disease to warrant inclusion here.

From these I have selected for discussion those that at present seem to be of considerable importance to clinical medicine, or about which there is new and interesting knowledge. However, before proceeding with that discussion I wish to clarify the use and meaning of certain terms. The term "nutritional deficiency" has two meanings depending on whether one is referring to a deficiency in the dietary, or the intake of food, or whether one is referring to the state of nutrition of the body. In health the body possesses a reserve of nutrients. Therefore, it is possible for a dietary nutritional deficiency to exist without a state of nutritional deficiency in the body. Only when a pathologic change in structure or function has occurred can we speak of nutritional deficiency disease. Clear understanding and attention to this relation will prevent much confusion and misunderstanding.

\* \* \*

Two nutritional factors that have assumed a new and important place in clinical medicine during the war are the energy principle (calories) and protein. In 1897, just about fifty years ago, Dr. Frederick C. Shattuck<sup>1</sup> wrote a paper, "Diet in Typhoid Fever," in which he advocated the use of relatively large amounts of food in this disease. Although he lacked a knowledge of all the underlying biochemical processes that demand such treatment, his practice was sound and represents for most practical purposes the recently developed concepts of nutrition in relation to injury and disease.

Simple, idiopathic calorie-and-protein-deficiency disease is not ordinarily seen by physicians. On the contrary, conditioned deficiency of these factors is one of the most frequent, perhaps the most frequent, of all the nutritional deficiencies seen in practice. Yet far too little attention has been paid to them despite the existence for many years of the example of typhoid fever. Here, a severe infectious disease, with a long, debilitating course, a relatively high mortality and a prolonged convalescence, was converted into a much less severe, less fatal illness during which patients often gained weight, maintained good general condition and recovered more quickly by the simple provision of an adequate calorie diet. Why the medical profession, with this experience before its eyes, has been willing to accept the severe weight losses and debility accompanying other infectious diseases and illnesses as a natural and inescapable concomitant of those diseases is rather incomprehensible.

Although it is customary to distinguish between calorie and protein deficiency, I should like to present the thesis that, so far as disease is concerned there is only a deficiency of protein and that for all practical purposes starvation, aside from lack of vitamins and minerals, is protein starvation. Under ordinary circumstances a healthy person possesses some slight reserve of carbohydrate (glycogen) and a considerable reserve of fat, amounting roughly to 10 per cent of the body weight, sometimes much more. When there is a dietary deficiency of calories this reserve is drawn on and used for energy (calories). Only when the fat is all or nearly all gone does the draft on tissue protein begin, and only when this exceeds a certain as yet indefinite point does actual nutritional deficiency disease begin. Under some conditions, as we shall see, there may be a direct loss of tissue protein without reference to calorie levels. When, however, calories are inadequate this loss is increased.

Recent studies, especially those conducted during the war, have provided much new knowledge about this deficiency and emphasized its importance as a frequent and serious complication of a variety of diseases, ranging from certain kinds of trauma and injury to infections and infectious diseases. The circumstances and nature of the deficiency are as follows. Many kinds of injury and disease are accompanied by a negative nitrogen balance. This means that more nitrogen is excreted than is taken into the body in the form of protein. Even so simple a restriction as confinement in bed may produce this effect. The most striking and uncomplicated examples are seen in fractures of the large bones in previously healthy and well nourished persons. Under these circumstances the negative nitrogen balance stands out as a sharply defined abnormality clearly related to the acute injury and without any background of other disease or apparent cause. Accompanying the negative nitrogen balance there

and calorie deficit can be anticipated. This should be met by nitrogen and calorie intakes to overcome or minimize these deficiencies. Standardized regimes are useful, but mainly to indicate the amount and kind of food and route of administration. *They will not assure its consumption.* Varco<sup>5</sup> has recently published a number of excellent diets for this purpose in a variety of surgical conditions. In general, 3000 to 5000 calories and 120 to 150 gm of protein are necessary and advisable. As has already been said, experience has shown that in many cases it is not necessary or desirable to secure complete nitrogen equilibrium during the early and more marked stage of the catabolic reaction, the disadvantages and untoward results of attempting to supply huge amounts of protein outweighing the advantages. However, sufficient protein and calories should be administered to provide a high intake of nitrogen, overcome the calorie deficit and take full advantage of the beginning of the anabolic period, which will probably be hastened by this treatment.

When possible, this nourishment should be provided as ordinary food, supplemented when necessary by special feedings. Such supplemental feedings will be required in most cases. In general an attempt should be made to secure an intake of around 2500 calories and 90 to 100 gm of protein by ordinary meals. The need for care in preparation and serving of the food and for assistance to the patient in eating is very great, and on this depends much of the success of the procedure. Fortunately, after an adequate or satisfactory intake has been secured for a few days the appetite generally improves and many patients will voluntarily consume large quantities of food.

The additional requirements are met by supplements. These are most satisfactorily furnished as milk drinks, composed of milk with added skim-milk powder, or prepared casein, and glucose. A variety of satisfactory formulas have been devised. A typical one provides 28 gm of protein and 343 calories for each 240 cc. Therefore, three such feedings will add 84 gm of protein and 1029 calories a day, bringing the daily intake to over 3500 calories and 160-180 gm of protein if the regular meals are consumed. Special recipes for other high-protein foods developed by the Medical Dietetic Division of the Army's Medical Nutrition Laboratory<sup>6</sup> are helpful in securing a high intake of protein.

The simplest guide in the management of these patients is loss of weight, which, except for the complication of edema, is quite a sensitive index of the state of protein nutrition. In general, it may be assumed that losses of more than 10 per cent below the ideal calculated weight are evidence of actual protein deficiency. However, in obese persons protein loss may occur before calorie deficiency and weight loss are apparent. Many patients are, of course, over their ideal weight and can tolerate larger losses of their actual weight so far as fat is

concerned. The metabolism of large amounts of fat, however, increases considerably the work of the liver, and in some circumstances, especially those in which there may be injury to the liver, this may not be desirable. This is particularly true in view of the recent evidence of the greater susceptibility of the liver to injury in conditions of protein deficiency.

Accurate nitrogen-balance studies are not often needed in these patients. A careful record of intake — calories and nitrogen — should be maintained in such patients, and it can be assumed that if intakes of around 3500 to 4000 calories and 120 to 150 gm of protein are secured the nitrogen deficit will be abolished or minimized in most cases. Losses beyond about 10 per cent of calculated ideal body weight should be avoided, and if losses exceed this figure a more careful determination of the nitrogen balance should be made. In burned patients, particularly, and in those with exudates, draining sinuses, dysentery and other causes of abnormal loss of protein, a careful check of the probable balance must be made to determine the necessary intake, which in some cases may be unusually large. For instance, it has been calculated that an average-sized man with a third-degree burn of 50 per cent of his body surface may lose as much as 199 gm of nitrogen in twenty-four hours from the burned surface, equivalent to 124 gm of protein. To replace this loss requires 600 gm of meat, or about 2000 cc of plasma, and the amount estimated to be necessary to put some patients in nitrogen equilibrium has been calculated to be as much as 2000 gm of meat, or 23 units of plasma.<sup>7</sup>

Particular attention must be paid to edema because of its nutritional significance and because it masks an actual loss of tissue. Retention of 10 pounds of water can occur without visible edema. Except in patients with complicating renal or cardiac disease, the edema is nearly always related to hypoproteinemia, which can be detected by determining the concentration of the plasma proteins. Ordinarily the determination of the total serum proteins by the simple specific-gravity methods suffices as a general guide, but the greater significance of the albumin and the possibility that albumin is depressed while total protein remains normal or near normal make it necessary to determine serum-protein fractions when such a condition is suspected.

With patients who are already in a state of nutritional-deficiency disease, more strenuous treatment is necessary because the problem is one of replacement rather than prevention — the replacement of losses rather than maintenance of reserves. Furthermore, speed is highly desirable, and delay merely prolongs recovery and convalescence. Weight, with due consideration for edema, is again the best general evidence of the state of protein nutrition and the loss of protein from the tissues.

These changes have recently been carefully studied experimentally by Keys and his associates.<sup>4</sup> Keys's subjects had only simple protein deficiency, but the effects so far as loss of protein from the tissues and organs is concerned are basically similar to those seen accompanying injury and disease with a primary negative nitrogen balance. In Keys's experiment previously healthy men were given about half the calories they expended daily, a regime designed to reduce their weight by about 25 per cent in a few months. In these subjects, in addition to the severe loss of weight, muscle atrophy, weakness and mental changes, there occurred edema, great atrophy of such viscera as the heart and physiologic changes, such as severe hypothermia, bradycardia and lowered basal metabolism.

In patients with injury or disease many of these abnormalities are even severer. Others are masked or modified, and not necessarily in a favorable way, by various factors not present in simple starvation. For instance, fever and infection prevent bradycardia and maintain or elevate the basal metabolism. The weakened heart may be enlarged instead of smaller. Edema is often greater and more dependent on hypoproteinemia. In Keys's cases the edema failed to show a close relation to plasma protein levels, and it is probable that other factors were concerned in its production, the likeliest one in my opinion being loss of tissue pressure resulting from the rapid and severe loss of weight. In patients, on the other hand, the nutritional edema is usually associated with a hypoproteinemia, often severe.

These, then, are the changes and the cause of the changes that produce much of the picture of serious illness so well known to physicians. They increase mortality, increase morbidity, predispose to complications, prolong the course of illness and delay convalescence and recovery. If they can be prevented or relieved, the course of disease becomes shorter and less severe, complications fewer, and the outcome more favorable. Reference has already been made to the possibility that the negative nitrogen balance occurring in injury and disease constitutes a protective and favorable reaction, and that therefore it may be inadvisable to suppress or abolish it. This is possibly true, and the difficulty or even impossibility of overcoming the negative balance early in the catabolic phase, nitrogen being excreted as fast as it is taken in, supports such a concept. Nevertheless there are many examples of reactions to disease, primarily beneficial, that when excessive become harmful and retard recovery. It seems improbable that protein losses to the point of severe weakness, muscle atrophy and hypoproteinemia can be beneficial, and experience suggests that measures to relieve, if not completely abolish, this reaction shorten it, hasten and strengthen the phase of recovery and prevent or minimize the untoward

effects of this reaction. Much attention is being paid at the present time to early ambulation, but early ambulation is useless, or even harmful or impossible, unless a proper state of nutrition is maintained or secured.

From this discussion it is apparent that in practice there are two stages of this reaction that can be rather sharply differentiated and that differ in their practical management. The first is the initial period when only the metabolic disturbance is present and no nutritional-deficiency disease has occurred. When the patient is seen in this stage there is the possibility of preventing or minimizing serious effects. The second is the stage when a greater or lesser deficiency has developed. In many cases this condition has developed under the eyes of the physician, and either it is ignored or the more difficult process of treatment rather than prevention is attempted.

As for the practical management of this problem and the maintenance or restoration of the proper nutritional state, I fear I must promise you Churchill's prospect of "blood, sweat and tears." Most of you, if you make an honest attempt to secure the benefits of such a regime, will sweat blood and weep tears. The principle is simple and easy. No difficult, highly specialized or expensive techniques or materials are necessary. But perhaps because of this, and because it does require close attention and supervision on the part of the physician and the nursing and other staffs, as well as the wholehearted co-operation of the patient, in the drab day-by-day business of getting food into the patient, it is a difficult problem. That it *can* be solved is shown by the success in the modern treatment of typhoid fever.

Much help can be derived from the use of standardized procedures or "routines," particularly in a hospital. However, as always, each patient will present an individual problem, his requirements will differ as will his response, and he will need individual attention. Routines can provide only the basic framework of the procedure, within which adjustments must be made for each patient.

A patient when seen by the physician should have an appraisal of the state of nutrition, the probable effects of the disease on his nutrition and what is needed for the prevention or treatment of nutritional disease. Often this will require only the usual history, physical examination and routine laboratory work, but special laboratory tests may be needed. For the patient who is injured or develops an illness in a normal state of nutrition, the need can be determined in general from the nature of the illness and its severity and probable duration, but complications and variations in the response of the patient and his co-operation may require modification from time to time. For instance, in fractures of the large bones, or severe trauma, in serious burns and in most major surgical operations for acute diseases, an immediate negative nitrogen balance



women who have failed to establish an adequate reserve during pregnancy, or who have even suffered from an actual protein deficiency, this additional protein loss may be a serious drain

Recent studies indicate a close relation between nutrition, particularly protein nutrition, and the toxemias of pregnancy. For example, Tompkins<sup>9</sup> found four times as many toxemias of pregnancy in a group of women with dietaries limited in protein as in those on a diet containing 110 gm of protein daily, five times as many with edema, and eight times as many with pre-eclampsia. In 1400 pregnant women Holmes<sup>10</sup> found twice as many with toxemias of pregnancy in those with protein intakes of 60 to 70 gm as among those with intakes of 110 to 120 gm. Edema is much oftener due to protein deficiency and hypoproteinemia than to renal or cardiac disease, and some cases of the anemia of pregnancy may have the same cause. Thus, the greater need for protein during pregnancy and the harmful effects of an actual protein deficiency require that protein be furnished in larger amounts at this time. Intakes of at least 1.5 gm per kilogram of body weight should be provided, and somewhat larger amounts are probably desirable. During lactation the intake should equal 2 gm per kilogram.

Two other aspects of protein nutrition of clinical importance in both primary and conditioned deficiency disease received attention during the war. One is the relation of protein to the formation of immune bodies. These substances, which are of vital importance in resistance to infectious disease, are contained in the gamma-globulin fraction of the serum proteins and are elaborated by the globulin-producing cells of the liver and reticuloendothelial tissue. In their formation protein is required, and moreover protein containing the essential amino acids. When the amount of such protein in the diet is inadequate, it can be derived for a time from the body tissues. But, when actual protein deficiency occurs and atrophy of the tissues ensues, production of the immune bodies becomes inadequate. Even the production and activity of the phagocytes is impaired, and this second defense against infection is weakened.<sup>11</sup>

The other aspect of protein nutrition is the action of the specific amino acids. Since some ten of the amino acids cannot be synthesized by the body and must be obtained in the food or some other exogenous source, it is obvious that deficiencies of these nutrients must occur. As yet, however, there is no known recognizable clinical expression of such deficiencies. We do know, however, that unless these amino acids are present in adequate amounts it is impossible to maintain nitrogen equilibrium, and there is a loss of nitrogen from the body that probably represents the breakdown of some body protein to supply the amino acid for a more essential purpose. Thus there occurs again a loss of protein from the tissues, which, if great enough and long enough

continued, must result in protein deficiency. Therefore it is necessary, in applying protein to prevent or relieve protein deficiencies, to provide protein containing adequate amounts of the essential amino acids.

It is also known that certain amino acids, notably methionine, are utilized in certain processes in the liver concerned with detoxification and that an adequate supply of protein containing such amino acids probably protects the liver against injury in certain endogenous and exogenous intoxications, such as anesthesia,<sup>12</sup> as well as against the effect of certain diseases, such as infectious hepatitis. This protective action fails or is inadequate in cases of protein deficiency.

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Turning now to the vitamins, deficiencies of vitamin A are often neglected in medical practice because of the rarity of xerophthalmia, outspoken night blindness or a severe dermatosis. Perhaps the erroneous concept of vitamin A as the anti-infective vitamin has given it a bad name among doctors. Vitamin A is not per se anti-infective. However, vitamin A deficiency is fairly frequent. Although in a recent review it is stated that it is probably infrequent in this country,<sup>13</sup> a report from Holland in the following issue of the same journal refers to it as the only vitamin deficiency that was observed in a great number of children.<sup>14</sup> It is the only vitamin deficiency, aside from rickets, commonly seen in Germany and Austria at the present time and has been rather prominent in France, Spain and other European countries. Although the signs and symptoms of the deficiency are not specific, they are suggestive and can be supported by determination of vitamin A concentration in the blood. Distinctly low values for the latter, in the absence of temporary causes, can be considered indicative of vitamin A deficiency from a practical clinical point of view.

Vitamin A is particularly important in pregnancy. The child is dependent on the mother for its supply, and the drop in blood vitamin A seen in the latter months of pregnancy<sup>15</sup> may represent in part the transfer from mother to child. If the mother's supply is low, she may deplete her own store and yet fail to furnish the infant with a sufficient store. When breast fed, the child is dependent on the mother's milk for an increase in its store of vitamin A, which is normally less than that of adults, gradually increasing as the child grows. An inadequate endowment may fail to be improved or even maintained if the child receives an inadequate postpartum supply from its mother, a serious deficiency because vitamin A is important in the growth of children. Fortunately, the widespread use of fish-oil supplements in this country, mainly to prevent rickets, tends to prevent greater deficiency of vitamin A among our children, an important reason for

Muscular atrophy supports this finding. Hypoproteinemia indicates the cause of edema, and its degree is a rough index of the degree of protein loss and atrophy of the other body tissues and organs as well as of the plasma. Intakes as high as 5000 to 6000 calories or higher and 200 to 300 gm. of protein may be required and very effective, although often somewhat smaller amounts suffice.

In patients with nutritional disease already established and in some other circumstances, the ordinary intake of food by mouth proves inadequate and parenteral feeding may be necessary. It may also be necessary in delirious or mentally ill patients, in those with disease of the gastrointestinal tract, especially as a preoperative procedure when haste is necessary or desirable, and for those who do not co-operate by ingesting adequate amounts of food. Ordinarily, parenteral feeding is best accomplished by stomach or duodenal tube, which can be used intermittently or for a continuous drip. For this purpose a variety of formulas for liquid foods are available, most of them similar to those used for supplemental feeding by mouth. There is, however, one valuable and notable addition—solutions of amino acids. These preparations, although very unpleasant when taken by mouth, are well tolerated if given by gastric or duodenal tube, are very efficient in replacing protein and make it possible to introduce large amounts of nitrogen with relative ease. Only solutions known to be satisfactory and capable of maintaining nitrogen balance when constituting the only source of nitrogen should be used.

In some cases it may be necessary to use intravenous feeding, alone or in combination with gastric or duodenal gavage. Ordinarily such intravenous feeding is only for replacement of nutrients lost acutely, such as in operations or trauma, and includes red blood cells, plasma, fluid and electrolytes. It is assumed in this discussion that such replacement of acute losses has been made. Occasionally, however, intravenous feeding is necessary for the maintenance or restoration of nutrition. For this purpose plasma or a solution of amino acids is used for nitrogen, and glucose for fuel. Nitrogen and calorie balance can be maintained by these means. However, except for replacement of acute losses, plasma is relatively ineffective. In existing states of protein deficiency and in many cases of burns and other diseases with large protein losses, the requirements are so great that it is physically impossible to satisfy them with plasma. Solutions of amino acids meet this objection and provide a fairly satisfactory means of restoring and maintaining nutrition over relatively long periods. There are numerous drawbacks to intravenous feeding, however. One is the amount of fluid necessary, which may overtax a weak heart, cause circulatory failure, induce or exaggerate edema and even provoke pulmonary edema and secondary pneumonia. Thrombosis of the veins used for injection occurs and may

interfere with prolonged feeding. The psychological influence of eating is lacking. Therefore intravenous feeding, particularly by itself, should be used only after careful consideration of the need and suitability, and for no longer than necessary.

Nothing has been said of vitamins and minerals, which are ordinarily less important to these patients than calories and protein. They will be discussed elsewhere. Except perhaps in burned patients they present little difficulty in previously healthy individuals. Adequate amounts for maintenance should be assured, and if these amounts are not available in the food they should be provided as supplements. In particular, provision should be made for adequate amounts of those vitamins directly concerned with cellular oxidations—thiamin, riboflavin and niacin—when patients are maintained on large intakes of pure carbohydrates, such as glucose, that carry with them no complementary vitamins. When given parenterally somewhat larger doses of these vitamins should be given than normally required because of greater excretion. In previously ill patients, or those seen for the first time with nutritional-deficiency disease, an appraisal should be made of their status in respect to vitamins and minerals and adequate restorative and maintenance treatment should be instituted.

Before leaving the subject of protein nutrition I should like to speak briefly of another condition that has a close similarity to injury and disease so far as liability to protein deficiency is concerned. I refer to pregnancy. The basis for the similarity is as follows. During pregnancy there is normally a positive nitrogen balance occasioned by the need of protein for the products of conception, and probably some for storage against the demands of lactation. If this requirement is not met by the food, the needed amount is taken from the mother's tissues. Thus there occurs a condition similar to the negative nitrogen balance of disease and injury, and if it is anything but minimal and if it continues for anything but a few days there will occur, just as in fractures, burns or typhoid fever, actual protein-deficiency disease. Also, as in fractures and burns, secondary factors may complicate and exaggerate the deficiency in pregnancy. Vagaries of appetite, nausea and vomiting, misinformed restriction of diet and such factors may all have such an effect.

Following delivery there is a negative nitrogen balance. In part this is due to involution, the excess nitrogen coming from the genital organs and tissues. But there may be still another loss, that of lactation. It has been estimated that during lactation 2 gm. of nitrogen is needed every day for every gram of nitrogen in the milk if nitrogen equilibrium is to be maintained.<sup>8</sup> Loss of blood during delivery constitutes an additional nitrogen loss. Unless sufficient protein is taken in to replace these losses, the protein must come from the maternal tissues. In those

women who have failed to establish an adequate reserve during pregnancy, or who have even suffered from an actual protein deficiency, this additional protein loss may be a serious drain

Recent studies indicate a close relation between nutrition, particularly protein nutrition, and the toxemias of pregnancy. For example, Tompkins<sup>9</sup> found four times as many toxemias of pregnancy in a group of women with dietaries limited in protein as in those on a diet containing 110 gm of protein daily, five times as many with edema, and eight times as many with pre-eclampsia. In 1400 pregnant women Holmes<sup>10</sup> found twice as many with toxemias of pregnancy in those with protein intakes of 60 to 70 gm as among those with intakes of 110 to 120 gm. Edema is much oftener due to protein deficiency and hypoproteinemia than to renal or cardiac disease, and some cases of the anemia of pregnancy may have the same cause. Thus, the greater need for protein during pregnancy and the harmful effects of an actual protein deficiency require that protein be furnished in larger amounts at this time. Intakes of at least 15 gm per kilogram of body weight should be provided, and somewhat larger amounts are probably desirable. During lactation the intake should equal 2 gm per kilogram.

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the use of fish oil concentrates rather than preparations of vitamin D alone at this period of life

Vitamin A deficiency is to be expected in diseases leading to faulty digestion, particularly of fats. It is found also in jaundiced states, because lack of bile hinders absorption, and in various forms of parenchymatous disease of the liver, in which the deficiency may be due to a failure to convert carotene to vitamin A or to store the latter. Recently vitamin A has become of interest in clinical medicine in another way. Vitamin A-tolerance tests, — similar to the glucose-tolerance test, — especially when combined with similar determinations of blood carotene, are useful in the diagnosis of sprue, celiac disease and diseases of the liver of various kinds. The blood levels of carotene and vitamin A are particularly useful in the differential diagnosis of sprue and pernicious anemia, the carotene being low in sprue and normal in pernicious anemia, with vitamin A usually low in sprue and normal in pernicious anemia. Ruffin and Wise<sup>16</sup> have recommended the vitamin A-tolerance test to distinguish between various kinds of hepatitis and obstructive jaundice, tolerance being low in the former and normal in the latter. A high concentration of plasma carotene with a low concentration of vitamin A suggests a failure of liver function. Of even greater interest are preliminary observations of Darby and his associates<sup>17</sup> at Vanderbilt, which suggest that vitamin A tolerance may be a more sensitive indication of recovery of liver functions in infectious hepatitis than such tests as cephalin flocculation.

A deficiency of ascorbic acid is one of the more frequent vitamin deficiencies seen in medical practice, although actual scurvy is uncommon. However, to wait for the appearance of scurvy before considering the possibility and significance of this deficiency is unwise. The pathologic changes of scurvy are progressive, their extent and severity depending on the degree and duration of the deficiency. Before the classic changes of scurvy are observed, less severe but nevertheless harmful lesions must have developed. It is true that scurvy, or even minor deficiency signs, may not appear in subjects experimentally kept on virtually zero intakes for months. This situation, however, is different from that of the patient who for many months or for years has failed to consume adequate amounts and who may have had an inadequate absorption or utilization or a destruction of the vitamin. Because of the frequency of conditioning or predisposing factors in medical practice, doctors should not be misled by misinterpreting data from studies on normal subjects.

Among the most recent findings in regard to vitamin C metabolism, a result of research during the war, are observations such as those of Andrae and Browne,<sup>18</sup> who found a high ascorbic acid retention in patients with thermal burns and fractures. This they believed could not be attributed to pre-existing

deficiency, faulty absorption or impaired excretion, retention in the tissues or edema fluid, or excretion in the form of dehydroascorbic acid. Although the exact significance of these observations is not clear, the large doses of the vitamin retained during the first week of such illnesses suggest the desirability of treatment with large doses of vitamin C in these cases.

Among the vitamin B complex factors, the frequency of thiamin deficiency has, in my opinion, been greatly overestimated and the use of thiamin in practice has been grossly excessive. To begin with, the human requirements for thiamin have been shown to be less than was previously believed. The "recommended allowances" of the National Research Council's Food and Nutrition Board have recently been reduced, and there is good evidence that amounts even considerably less are not accompanied by any recognizable alteration in either nutritional status or physical and psychomotor performance. A source of confusion and error concerning the frequency of thiamin deficiency is mistaken diagnosis in patients said to have beriberi, especially of the wet type, in whom the distal tendon reflexes and the vibratory and other sensory functions are perfectly preserved, and in whom there are no localized muscle weakness and no muscle atrophy. This error has been increased by the erroneous belief that requirements for thiamin are increased in certain environments, such as that of the tropics, and in part by increased excretion in the sweat, neither of which is true. It is interesting that with all the dietary deficiencies that have accompanied the war and involved large populations, thiamin deficiency, except in certain regions in the Pacific and the Far East, has been conspicuous by its rarity. The explanation is found in the long extraction of bread grains that goes with food shortages and the frequent use of various legumes to eke out the supply of flour. The more frequent occurrences in the Pacific seem to be due to the persistence of the custom of using polished rice even when the supply of rice is inadequate. In the Chinese troops I examined, the absence of beriberi was always associated with the use of unhusked rice.

Nevertheless, deficiencies of thiamin do occur, and it must be remembered that slight dietary deficits long continued will eventually deplete the reserves, leaving the person dependent on current intake, which may be sharply reduced by various conditioning factors. Keys and his associates<sup>19</sup> have shown that, although human subjects can be maintained in good condition for weeks on amounts in the neighborhood of 0.22 mg per 1000 calories, a sudden drastic reduction below that level is quickly followed by serious manifestations of deficiency.

One of the newer clinical observations during the war was the finding of a rather large number of cases of severe optic neuritis and, apparently, of neuritis of the eighth nerve caused by thiamin deficiency.

These lesions are, however, apparently encountered only in severe and long-continued deficiency. In ordinary practice they are seen rarely, usually in alcoholic patients.

Although the signs of early or mild thiamin deficiency are not particularly reliable, a near-zero urinary excretion or an extremely poor response to a test dose of the vitamin can for ordinary clinical purposes be considered as indicative of at least a depleted and vulnerable state of thiamin nutrition. In the more acute and severe deficiencies that may suddenly supervene in chronic mild deficiencies, the pyruvic acid concentration in the blood may add helpful evidence if complicating factors of exercise or other disease are eliminated. Diagnosis of a deficiency of thiamin should not ordinarily be made if there is a good urinary excretion of the vitamin.

An important development in respect to riboflavin has been the accumulating evidence of the nonspecificity of some of the manifestations attributed to a deficiency of this vitamin. The latest has been the demonstration by Darby<sup>20</sup> that perleche and the glossitis attributed to riboflavin deficiency may respond dramatically, at least in some cases, to the administration of iron, the state of iron deficiency being established by demonstrating a large absorption of radioactive iron (Fig. 1).

Undoubtedly the most important recent development in relation to niacin (nicotinic acid) and pellagra has been the finding of Elvehjem and his associates of the relation of niacin metabolism to the amino acid tryptophane. In their original report these authors<sup>21</sup> showed that the niacin requirements of rats are apparently greatly increased by the feeding of large amounts of corn. Subsequent studies have shown that the effect is due to the low tryptophane content of the diet, and that the addition of tryptophane increases the bacterial synthesis of niacin in the intestine and enables the animal to grow despite a low dietary intake of niacin.<sup>22</sup> Changes in the carbohydrate of the diet have a somewhat similar effect, dextrin favoring the synthesis of niacin, and sucrose lessening it. Although these studies were confined to rats and their significance for man is not fully established, they are cited because they indicate the possibly important role of intestinal bacterial synthesis of vitamins in human nutrition.

The newest vitamin shown definitely to be related to disease in man is a member of the vitamin B complex, the so-called "*L. casei* factor" or folic acid. Previous studies with animals had shown it to be related to diarrhea and anemia in monkeys, under the designation vitamin M,<sup>23</sup> and later to anemia, leukopenia and agranulocytopenia in rats.<sup>24</sup> The material was synthesized in 1945.<sup>25</sup> Later in the same year, Spies and his associates<sup>26</sup> reported that it caused a reticulocytosis, with increased red cells and hemoglobin, in certain human cases of macrocytic anemia that were not well defined by the au-

thors. At about the same time Darby, Jones and Johnson<sup>27</sup> reported that in patients with sprue there was a prompt relief of glossitis and stomatitis, cessation of diarrhea, a sharp reticulocytosis followed by an increase of red cells and hemoglobin, great gain in weight and strength, a return to normal of the glucose and vitamin A tolerance and a lessening of fat in the stools following the injection of 15 mg daily. Examination of the bone marrow showed a striking return to normal, with greatly increased



FIGURE 1 Photograph of a Patient with Glossitis and Perlèche (Angular Stomatitis)

This woman of forty-five, who had a hemoglobin level of 6.5 gm., was relieved by adequate doses of iron following demonstration of iron deficiency by measured absorption of radioactive iron.

maturation of the red cells. These findings have been amply confirmed. The material has been shown to be effective by mouth, and smaller, though definite, responses have been obtained with much smaller doses. In addition, it has been shown to be effective in anemias of the Addisonian type. Recently Darby and Jones<sup>28</sup> have observed a patient with pernicious anemia in relapse who responded with a reticulocytosis of some 25 per cent six days after receiving 3 mg of the vitamin daily by mouth (Fig. 2). This is the more remarkable because the degree of anemia in this patient was not such as to suggest a response of that magnitude from the use of the usual liver extract.

So far the exact relation of this vitamin to the antipernicious principle of liver, to the extrinsic factor of Castle and to other aspects of pernicious anemia is not clear. It is apparent, however, that

we have in this vitamin a powerful agent for the relief and prevention of serious macrocytic anemias, sprue and possibly some disorders of the leukocytes

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Anemia related to folic acid deficiency is not the only anemia caused by nutritional deficiencies. A frequent nutritional anemia is iron-deficiency anemia. This is, in fact, one of the commonest nutritional diseases seen by doctors in this country,

may fail to meet demands. In adults, loss of blood from any one of a great variety of causes — chronic bleeding hemorrhoids, metrorrhagia, peptic ulcer, frequent pregnancies (complicated by a contribution to the fetus) and surgical operations — may reduce the reserve to a point that makes it impossible to restore normal levels of hemoglobin.

From a dietary and nutritional point of view it is important to note that an anemia of this type will not respond to dietary iron alone. Pharmaceutical

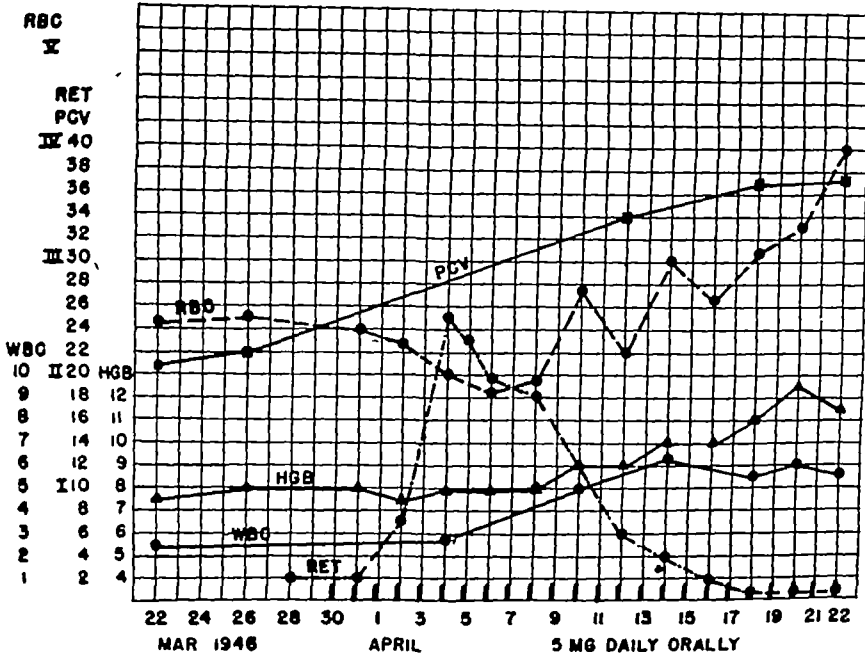


FIGURE 2 Response to Orally Administered Folic Acid  
This chart shows the reticulocytosis and response of red cells and hemoglobin to a daily dose of 5 mg of synthetic L casei factor (folic acid) by mouth in a woman of sixty-three

despite the fact that it is found principally in children and women

Iron-deficiency anemia is almost always a conditioned deficiency in adults, and in them is rarely due to a dietary deficiency of iron alone. The body conserves iron so carefully that almost none is lost except by hemorrhage and, in females, by transfer to the fetus. Children require iron for growth in addition to the endowment they receive from their mothers at birth. From this it is apparent that iron-deficiency anemia occurs under the following circumstances: failure of a normal endowment, intakes inadequate to meet the demands of growth, and hemorrhage. Actually the first two of these mechanisms are often combined. The mother furnishes from her own store, and at its expense, iron for the hemoglobin of the fetus. But with inadequate stores of her own she may fail to endow the infant with sufficient reserve. Growth requires additional amounts, and with an inadequate dietary intake

preparations of iron must be given in adequate doses. These are the reasons why iron-deficiency anemia is so particularly a responsibility of the doctor. Its development is almost entirely due to conditions with which he is directly concerned, its cure requires his services. All this is known to most of us, but the surprising thing is the number of people at the present time with this disease, sufficient to interfere with their health and efficiency, in whom it is not recognized and not treated. Patients with a history of loss of blood are operated on, they lose more blood, they receive one or more transfusions and are finally discharged convalescent with the hemoglobin returning to normal. But it does not reach normal, and a surprising amount of ill-health continues. The proof of the cause of the ill-health is the demonstration of an uptake of iron characteristic of iron deficiency, a response of the blood to adequate doses of iron and a relief of symptoms. Clinically this is shown by a significant reticulocytosis.

This concludes my discussion of some of the phases of nutrition that concern medical practice. If I have dwelt overlong on protein nutrition, it is because I believe that it is the major problem of nutrition in clinical medicine today. On the successful prevention and treatment of this nutritional deficiency disease depend a tremendous improvement in medical care, a great decrease in mortality and morbidity from injury and trauma and from disease and illness of many kinds and great advances in the management of pregnancy, and in child health and development. Other nutrients and nutritional deficiencies are important, and their control will contribute to the improvement in health. By careful individual attention to nutritional requirements and to the prevention or cure of nutritional deficiencies, their ill effects, both primary and on the course of other injury and disease, may be prevented. It is not, however, a thing that can be accomplished without effort. Only if the physician devotes as much attention, relatively, to this as he does to other phases of the care of the sick and injured can he hope to gain for himself and his patients the benefits that our modern knowledge of nutrition has to offer.

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# THE USE OF THE SOUTH AFRICAN FROG (*XENOPUS LAEVIS*) IN THE DIAGNOSIS OF PREGNANCY\*

S L ROBBINS, M D,† F PARKER, JR, M D,‡ AND W C DOYLE, A B §

BOSTON

THE use of the South African clawed frog (*Xenopus laevis*) in a test for pregnancy was first reported some years ago,<sup>1, 2</sup> only five years after Aschheim and Zondek's original description of the mouse test in 1929.

Like its predecessors, the test is based on the stimulation of the ovaries by the gonadotropic hormones excreted in the urine of pregnant women or of persons harboring neoplastic chorionic tissue

eight hours and usually within twenty-four hours. The clinical importance of this relative speed is obvious in diagnostic problems, such as in threatened rupture of tubal pregnancy and in certain other surgical conditions. Since the frog reacts to a positive test by the extrusion of hundreds of eggs, the simplicity of reading the test is apparent (Figs 1 and 2), obviating the necessity, as in the rabbit, rat or mouse tests, of surgery or sacrifice of the

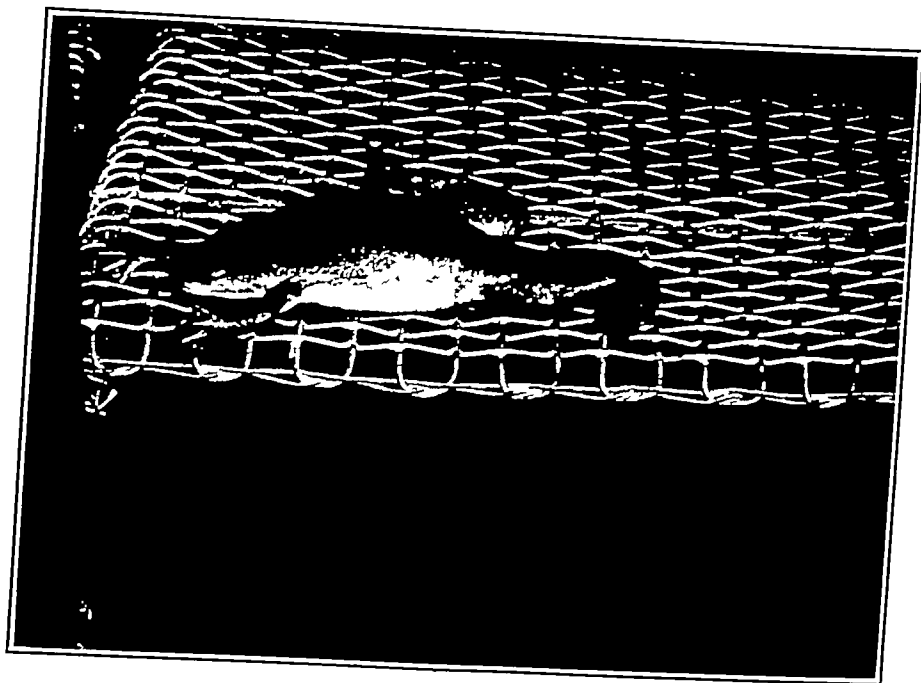


FIGURE 1 Negative Frog Test

The adult South African clawed frog is peculiarly suited for this procedure because its ovaries always contain eggs, which the frog never extrudes unless it is contacted by the male or unless the ovaries are artificially stimulated by gonadotropic hormones. The frog test has many significant practical and economic advantages over the Aschheim-Zondek and Friedman tests. Whereas the rabbit, rat and mouse tests require two to five days for their performance, the frog test can be read often within

animals to visualize the ovarian changes. In addition, the histologic technics employed in other tests are completely unnecessary in this procedure. The frogs can be used over and over again with thirty days' rest after a positive test and with five days' rest after a negative test. Since these animals cost \$6 apiece and have an active reproductive life of ten to twelve years, the cost of performing each test is rendered appreciably lower than that of other methods in which the use of experimental animals is limited to a single observation or at best to three or four observations. All these factors, together with the ease in maintaining and feeding the frogs, make them wholly satisfactory diagnostic animals for pregnancy tests.

\*From the Mallory Institute of Pathology, Boston City Hospital.

†Assistant pathologist, Mallory Institute of Pathology; assistant professor of pathology, Boston University School of Medicine; instructor in pathology, Tufts College Medical School.

‡Pathologist-in-chief, Mallory Institute of Pathology; associate professor of pathology, Harvard Medical School.

§Laboratory assistant, Mallory Institute of Pathology.



The accuracy of the clawed-frog test, in comparison with that of the older, more widely accepted technics, is perhaps the most important factor. During the past year, over 100 urine specimens have been tested by this method at the Mallory Institute of Pathology. In every case the urine used was one of the routine specimens received daily at the laboratory. It is the purpose of this paper, in addition to emphasizing the many advantages of the clawed-frog method, to report on its reliability in the routine diagnosis of pregnancy.

#### TECHNIC

As was previously mentioned, the technic for the performance of the test is extremely simple. Eighty cubic centimeters of the first morning urine is required

until at least twenty-four hours has elapsed. It is worth mentioning that cases with suspected low hormone titers, such as may be encountered in very early pregnancy, incomplete abortion or a blighted ovum, can frequently be detected by the concentration of larger volumes of urine (160 cc.), the same procedure as outlined above being used and the final sediment being dissolved in the same volume of saline solution.

#### RESULTS

For the sake of comparison, the 100 cases in this series have been divided into four groups — those of possible normal pregnancy, those of suspected ectopic pregnancy, those in which the patient was in the process of miscarrying and the problem of

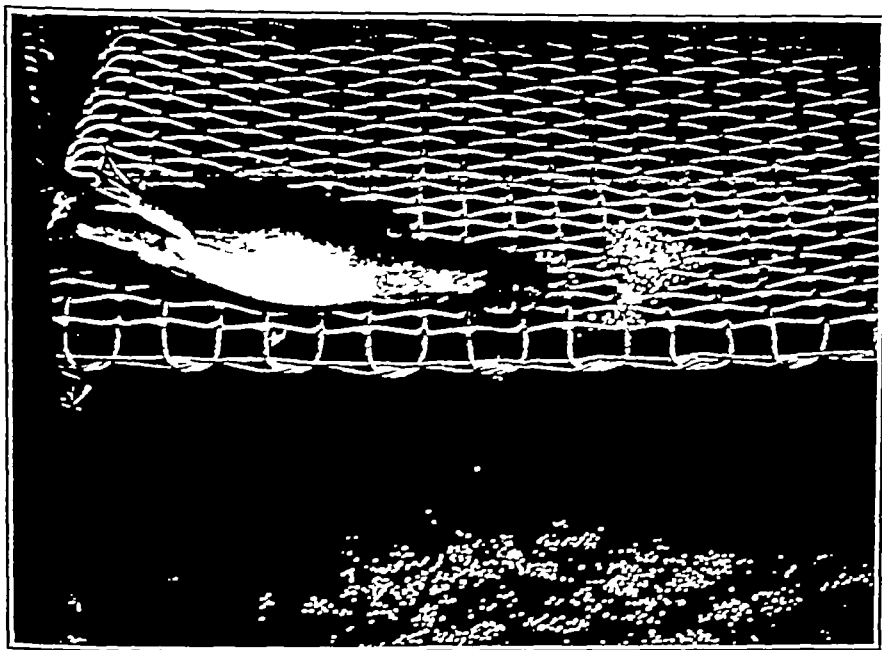


FIGURE 2 Positive Frog Test

*Note the numerous eggs on the screen and the floor of the tank*

for concentration.<sup>3</sup> To this amount is added double the volume of acetone, and the precipitate is spun down in a centrifuge. The supernatant is discarded, and the sediment is washed once or twice with ether by resuspension and centrifugation. After being dried, the material is dissolved in 2 cc of normal physiologic saline solution, the reaction is adjusted to pH 5.5, and 1 cc. of this concentrate is injected into the dorsal lymph sac of each of two frogs. This method concentrates the hormones present in 40 cc. of urine into a volume of 1 cc. In most cases, a positive test, denoted by the extrusion of eggs, can be read within eight to twelve hours. A negative result, however, should not be assumed

the viability of the gestation hinged on the hormone level in the urine and those of obvious intra-abdominal tumor in which the possibility of concomitant pregnancy was entertained. In every case parallel control injections of urine were made into immature rats, following the procedure outlined by Aschheim and Zondek.

In the few cases in which the frog and the rat methods failed to agree, the clinical record of the patient was consulted. Where necessary, through the co-operation of the clinical services, repeated physical examinations and hormone analyses were made until no further doubt about the final diagnosis existed.

The results of the frog test are analyzed in Table 1 from the standpoint of correct or incorrect diagnosis. As the table indicates, in 4 cases the frog test gave false-negative results. In the 2 cases of miscarriage in which the reaction was negative, the clinical courses of the patients were practically identical and in both cases the urine sample had been obtained within hours of the actual passage of the fetus, as the following case indicates:

D McD., a 35-year-old woman, entered the hospital on May 11, 1945, because of the onset of irregular vaginal bleeding, with the passage of clots but no tissue or fetus. The last menstrual period had occurred on January 5. In March there was an episode of slight vaginal staining, which lasted for 2 days. In an effort to determine whether the fetus was still viable, a urine sample was taken on the day of admission. Several hours later the patient passed the fetus. When the urine was tested, the Aschheim-Zondek test was positive, and the frog reaction was negative.

In the 2 cases of ectopic pregnancy in which the frog test gave a false-negative result, the duration of the pregnancies at the time the urine specimens

to assume that the duration of gestation must have been not more than twenty days.

### DISCUSSION

As can be seen from the preceding results, no false-positive diagnoses were encountered throughout the series. This finding has been corroborated by many previous investigations.<sup>4, 5</sup> In 4 cases, the frog method gave a false-negative result. The clinical follow-up of these patients showed that in each case the hormone titer of the urine had undoubtedly been low. In the 2 cases of ectopic pregnancy, it is likely that the viability of the products of conception had been impaired, at least to some degree, before the urine sample was obtained, because an equally early ectopic pregnancy in another patient gave a clear-cut positive result with the frog test. In the other 2 cases in which the results with the frogs were incorrect, the patients were in all probability in the process of miscarrying at the time the urine was obtained, and with the death of

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Because of the persistence of the vaginal bleeding, a curettage was performed on June 10. The report was as follows: "Decidua-like cells, no definite chorionic villi." The lower abdominal pain persisted, and on July 6 an exploratory laparotomy revealed a left-sided tubal pregnancy. Three days later hormone tests were again performed, and both the rat and frog reactions were negative.

In contrast to this case, it is interesting to note that in another ectopic pregnancy not unlike it, in which the frog test was correct, the period of conception was only five weeks.

The shortest duration of pregnancy detected by the frog test occurred in the normal-pregnancy group and was positive five days after the first missed period. Since the patient followed a relatively exact twenty-eight-day cycle, it seems fair

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During the later stages of this series, with increasing experience, it became apparent that these inaccuracies could be avoided, in large part or entirely, by one of several modifications of the original technic, and in the last 78 cases of the series no discrepancies were encountered. Thus, on one occasion, when a pair of frogs received equal volumes of the same urine, one animal responded with the extrusion of eggs and the other frog failed to react, even after twenty-four hours had elapsed. After the passage of another twenty-four hours the latter frog became positive, demonstrating either an extremely low hormone titer in the urine, to which one animal was more sensitive than the other, or a sluggish physiologic response on the part of the late-reacting frog. Therefore, the rare false-negative result can often be avoided by observing all test animals for forty-eight hours.

In an effort to minimize further these false-negative reactions in cases of suspected low titer, we have recently resorted to the use of a concentrate from a larger volume of urine (80 cc.), and have as yet encountered no ill effects on the frogs. In the case of the twenty-day period of pregnancy, parallel

jections of a 40-cc and an 80-cc concentrate were made into two pairs of frogs. The animals receiving the larger volume reacted much more vigorously, giving strong positive reactions, whereas the other pair gave extremely weak positive reactions.

It is to be hoped that, with these larger amounts of urine, levels of hormone can be detected that will make the frog test compare favorably in sensitivity with the rat test. It must be acknowledged, however, that when the original technic is followed the frog, although never giving false-positive reactions, appears to be somewhat less sensitive than the immature rat. On the other hand, since adoption of the modifications mentioned above, false-negative reactions in urines of extremely low titer have been avoided.

### SUMMARY

The extrusion of eggs by the South African clawed frog on stimulation by mammalian gonadotropic hormones, such as are excreted in the urine of women during pregnancy, offers a desirable test for pregnancy. Among its advantages are speed, since ordinarily only eight to twelve hours are required for a positive reaction, ease in the performance and reading of the test, economy, since

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In a carefully controlled series of 100 consecutive routine urine analyses, the test gave no false-positive reactions, but in 4 cases of low-titer urines it failed to give a positive reaction. It is believed that with minor modifications in the original technic these false-negative reactions can be avoided and that this test can be made to compare favorably with the older, more widely accepted rabbit, rat and mouse tests. The rapid diagnosis that it affords is desirable in general, and in cases presenting difficult diagnostic problems this factor may be of great value in indicating the correct therapeutic procedure to be adopted.

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## THE ORAL LESIONS OF MONOCYTIC LEUKEMIA\*

### Report of a Case

FRANCIS P. McCARTHY, M.D.,† AND PAUL H. KARCHER, D.M.D.‡

QUINCY, MASSACHUSETTS

IN REPORTING this case of subacute monocytic leukemia, the oral lesions are particularly stressed, since they dominated the clinical picture almost from the onset of the blood dyscrasia.

Oral lesions represent a frequent and early finding in the various types of leukemia, especially in the acute forms. In monocytic leukemia, which represents 5 per cent of all the cases of leukemia, gingival and other oral changes occur in an extremely high percentage of cases except in edentulous mouths. Indeed, much of the suffering experienced by the patient in monocytic leukemia is related to the pain and discomfort from the necrotic and ulcerative lesions of the gingival and buccal mucosa, the highest percentage of lesions being found in the acute cases. Love<sup>1</sup> reported 82 of 152 cases of various types of leukemia with oral lesions. The most frequent sign was bleeding from the gums, with swelling, necrosis and ulceration of the gin-

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There are many other causes of gingival hyperplasia with edema, necrosis and a tendency to bleed from the gums, either spontaneously or from slight

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‡Senior oral surgeon, Quincy City Hospital.

trauma In the treatment of epilepsy with dilantin extreme cases of gingival hyperplasia, in many of which the teeth are completely obscured, occur in about 50 per cent of patients.<sup>6</sup> The hyperplasia develops principally on the labial aspect of the gingivae in these cases. In all cases of Vincent's infection of the gingivae, with its associated redness and necrosis and fetid breath, it is desirable to make an examination of the blood to rule out a severe blood dyscrasia. Aplastic anemia, agranulocytosis, infectious mononucleosis and reaction to many drugs may cause acute gingival necrotic lesions similar to the lesions found in leukemia. The blood picture, together with other physical findings, should enable

spleen were not palpable, and the chest was clear of rales. The white-cell count was 17,530, with 33 per cent mature neutrophils, 3 per cent metamyelocytes, 1 per cent myelocytes, 2 per cent myeloblasts, 1 per cent eosinophils, 28 per cent lymphocytes and 32 per cent monocytes, 2 histiocytes were seen. Oral examination revealed a marked hypertrophic condition of the gingival papillae. They were extremely soft and spongy and bled easily when touched. A sternal puncture yielded an almost pure culture of large monocytic cells, with an extreme reduction of the normal cellular elements of the marrow. A diagnosis of subacute monocytic leukemia was made. During the patient's stay the course of the illness was progressively downhill, although there were temporary responses to transfusions and injections of a bone-marrow stimulant. The patient ran a spiking temperature up to 102°F during the hospital course, and the gums failed to respond to radiation therapy.

On entrance to the Quincy City Hospital 3 months after the onset of the disease, the oral condition was further advanced (Fig. 1). The patient complained particularly of the

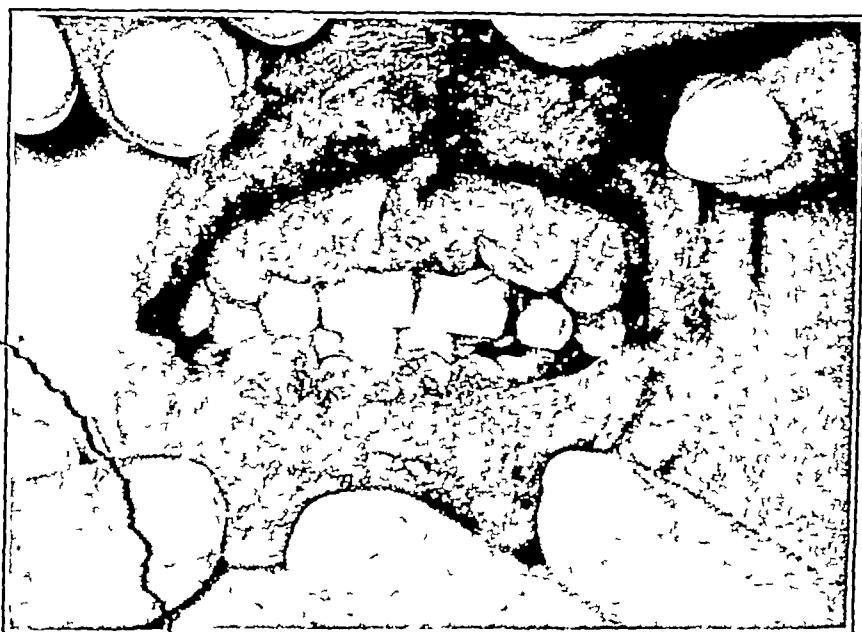


FIGURE 1 Photograph of the Teeth and Gums

*Note the marked hyperplasia of the gingiva, which almost completely obscures the lower cuspid teeth*

one to differentiate the etiologic factors in these cases

L. T., a 27-year-old woman, was admitted to the Quincy City Hospital on February 3, 1945. The family history was negative. The patient's parents, both of two brothers and a sister were living and well. She had had no previous serious illness and had the usual children's diseases at an early age.

Three months previously the patient had first complained of a severe headache, which was located in the orbital, frontal and occipital regions. There was an associated inflammation of the eyelids, with a slight exudate. There was chronic nausea with occasional attacks of vomiting almost from the beginning of the illness, and a weight loss of 50 pounds in 3 months. The patient was admitted to the Clinic Consultation Service of the Pratt Diagnostic Hospital on January 3, 1945, and was discharged on January 18. On entrance there she appeared quite sick, and in addition to bleeding and swollen gums showed swollen eyelids, with a mild conjunctivitis. Physical examination revealed marked emaciation, with extreme pallor of the skin. The liver and

pain and discomfort in the mouth. There was dysphagia and increased salivation but no bleeding from the gums. A pronounced fetid odor to the breath similar to the odor found in cases of acute Vincent's infection was present. There was a moderate swelling of the gums, which were bright red and edematous, with elongation of the interdental papillae. A superficial grayish slough was noted at the borders of the papillae, similar to that seen in acute Vincent's gingival infection.

Smears taken shortly after entrance revealed a rich bacterial flora, with Vincent's spirochetes and fusiform bacilli predominating. The teeth appeared to be in good condition, with the exception of the superior left 1st molar, which showed extensive caries. The buccal mucosa showed generalized reddening, but no areas of necrosis or purpuric lesions were noted. The cervical lymph nodes were moderately enlarged, especially in the submental and submaxillary regions, and palpation of these nodes elicited moderate tenderness.

There was progressive involvement of the tissues of the oral cavity until death, which occurred on March 14, in spite of local and constitutional treatment, including multiple

blood transfusions. The hyperplastic gum tissue increased in size along both the labial and lingual surfaces of the alveolus. The entire arch became broad and was made up of swollen, edematous, necrotic, vascular gingival tissue that gradually obscured the teeth. Three or 4 weeks after the initial examination, a secondary growth of hyperplastic tissue developed at the base, following the same pattern as the outer layer and increasing the width of the alveolus to such an extent that the palatal vault was all but eliminated. The floor of the mouth above the myohoid ridges was also partially filled with vascular, necrotic gingival tissue, so that the tongue was raised and there was inability to close the mouth.

The mouth remained extremely dry, partly owing to evaporation, and new superficial necrotic lesions of the mucosa developed, with secondary gangrenous changes. These areas, which were located on the lateral margins of the tongue and the buccal mucosa of the cheeks, were covered by a pale-yellow pseudomembrane, which on peeling left a raw, bleeding surface. There was an ulcerated lesion on the right lateral palatal region near the 1st molar tooth and another involving the left side of the soft palate and extending to the anterior pillar of the fauces. Four days before death, fairly generalized petechial and purpuric macular lesions appeared on the buccal mucosa, concomitant with similar hemorrhagic lesions of the skin over the face. Inspissated blood, mucus, detritus and exudate formed a hard shell on the dorsum of the tongue. This deposit was softened and removed daily. Following the formation of the secondary hyperplastic gum tissue, the teeth tended to migrate and to assume fantastic positions in the arch, indicating destruction of the alveolar lamina dura.

A biopsy specimen taken from an interdental papilla showed the following histologic picture. The outer labial stratified epithelial surface was thinned out, especially in the prickle-cell layer. There was considerable edema of the underlying tunica propria, with increased capillary vascularity. There was a wide zone of edematous fibroblastic connective tissue moderately infiltrated with monocytes and cells of the lymphoid type, with rare polymorphonuclear leukocytes. The monocytes represented 50 per cent of the infiltrating cells. Deeper in the specimen was less edematous and more pronounced cellular tissue, consisting principally of closely packed monocytic cells with a few lymphocytes. The large vessels were choked with monocytes. The dental surface of the gum tissue showed marked necrosis, with absence of the epithelial surface layer. The infiltration of monocytes was especially pronounced, and there were numerous foci of hemorrhage. This portion of the specimen represented the site from which a rich bacterial flora and Vincent's organisms were demonstrated on smears.

The local treatment to the oral cavity given by one of us (P.H.K.) consisted of irrigations with warm normal saline solution, which tended to keep the exudate softened and helped in removing the pseudomembrane from the necrotic surfaces of the gingival and buccal mucosa. This procedure was frequently used during the daytime and gave considerable relief from the pain and dryness in the mouth. Zinc peroxide dusted into the deep recesses of the necrotic and hyperplastic tissue, especially after eating, and neosarsphenamine in glycerin—0.8 gm to 30 cc of glycerin—swabbed into the necrotic pockets helped to control the secondary invasion of Vincent's organisms. Six-millimeter gauze strips saturated with oil esthesin, an oil-base surface anesthetic, placed in the superior and inferior vestibule of the mouth three times daily after eating controlled much of the pain. Hyperplastic necrotic and gangrenous tabs of tissue were cut away with a scalpel and curved scissors, giving much relief. Vaseline smeared on the lips and commissure kept them soft.

**Autopsy.** The body was that of a fairly well developed and poorly nourished young woman. The scleras and skin had a moderately icteric tinge. There were purpura and petechial hemorrhages on the face, especially the alae nasi, and the forearms. There were recent organizing fibrinous adhesions binding the right lung to the chest wall and obliterating the pericardial sac.

In the upper half of the lower lobe of the right lung, there were multiple milary abscesses surrounded by areas of consolidation up to 1 cm in diameter. Both the spleen and the liver were enlarged, and the malpighian bodies in the spleen were barely visible. The kidneys were remarkable in appearance. Their combined weight was 360 gm. Removal of the capsules revealed smooth, canary-yellow cortical surfaces

with an average thickness of 1.2 cm. The line of demarcation between the cortices and pyramids was barely discernible, and there were multiple petechial and large hemorrhagic foci throughout the parenchyma of both kidneys and also in the pelves. There was no evidence of adenopathy in the cervical, axillary and inguinal nodes.

Microscopic examination of the viscera revealed the following. **Kidneys.** The tubular epithelium took the stain extremely faintly, and many of the cells show only nuclear staining. There was a diffuse cellular infiltration of the connective tissue with monocytes and lymphoid cells. The convoluted tubules showed the most pronounced evidence of epithelial degeneration. Hyaline casts were demonstrated in the tubules throughout the specimen. The long, straight veins of the pyramids were congested. Focal areas of hemorrhage occurred in the cortex and pyramids. **Spleen.** The spleen showed a diffuse infiltration with monocytes and cells of the lymphoid type and rare eosinophils. Phagocytic cells containing brownish granular pigment were diffused throughout the pulp. The capillaries were dilated with focal areas of hemorrhage. The malpighian bodies were small and disorganized. **Liver.** The interlobular connective tissue of the liver showed a marked cellular infiltration, principally monocytic. The capillaries and sinusoids revealed similar infiltration. The capsule and subcapsular space showed an extreme monocytic cellular infiltration. The liver cells took the stain extremely faintly, and many contained vacuoles. There was a moderate proliferation of the bile ducts. Focal areas of hemorrhage occurred throughout the organ. **Lymph Nodes.** The architecture of the lymph nodes was obliterated, although the germinal centers of the lymph follicles were discernible. There was a diffuse infiltration of the nodes and capsules with monocytic cells and lymphoid cells (Fig. 2).

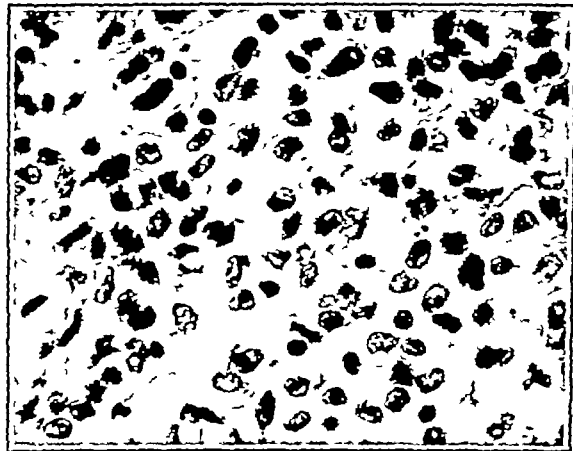


FIGURE 2 Photomicrograph of a Section of Lymph Node Showing Diffuse Infiltration with Monocytic and Lymphocytic cells

No polymorphonuclear leukocytes or eosinophils were demonstrated. **Bone Marrow.** The bone marrow of the rib showed a significant reduction in the normal cellular components. There was a marked increase in monocytes, which represented 80 per cent of the total cells. A few myelocytes, lymphocytes and nucleated red cells were demonstrated. **Blood.** A stained smear showed lymphocytes and monocytes, with relatively few polymorphonuclear cells (Fig. 3).

The anatomical diagnoses were as follows: subacute monocytic leukemia, acute hemorrhagic nephritis, fatty degeneration and infiltration of the liver, subacute adhesive pericarditis, splenomegaly, septic bronchopneumonia of the right lung, icterus, purpura hemorrhagica, hyperplastic stomatitis, with necrosis and purpura, ulcerative enterocolitis, monocytic hyperplasia of the bone marrow, and monocytic infiltration of the viscera.

Lesions of the oral mucosa with extensive involvement of the gingivae represent important complications in acute and subacute monocytic leukemia, particularly since much of the suffering is caused by them. It is desirable that the dental consultant

Treatment of these lesions by the dental consultant was helpful in relieving the acute symptoms in this case.

In monocytic leukemia, involvement of the oral cavity occurs more frequently than in any other

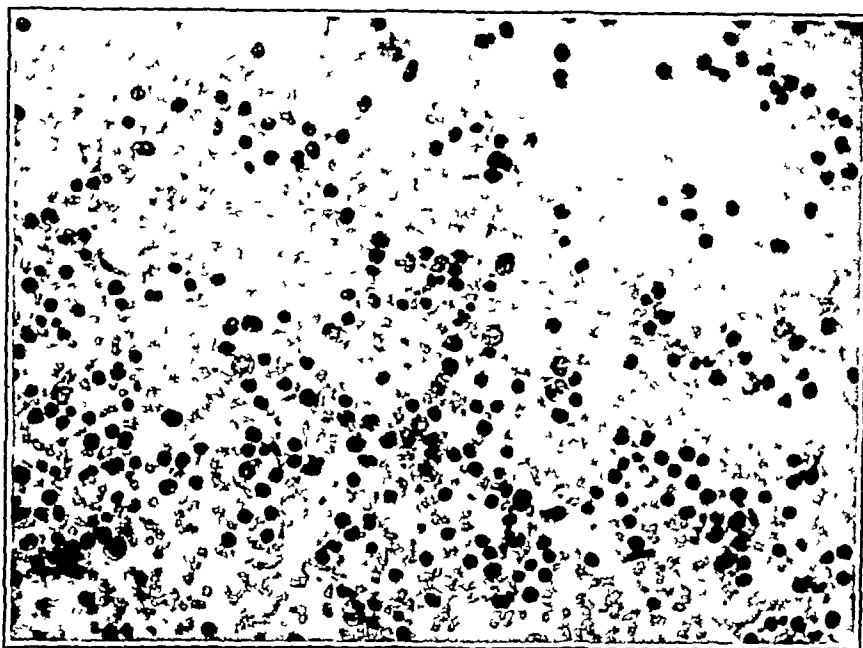


FIGURE 3 Photomicrograph of a Blood Smear Showing Lymphocytosis and Monocytosis but Relatively Few Polymorphonuclear Leukocytes

take over the management and treatment of the case as it relates to the mouth, and that he apply the treatment either personally or under direct supervision so that the patient may be relieved of the intense discomfort attending these cases. In all cases of gingival hyperplasia with bleeding and a tendency to necrosis, with secondary Vincent's infection, blood examinations should be made to rule out serious blood dyscrasias.

#### SUMMARY

A case of subacute monocytic leukemia is described, with special reference to the oral lesions.

type of leukemia and is often an early manifestation.

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## MEDICAL PROGRESS

## FLUORINE AND DENTAL CARIES (Concluded)

VLADO A. GETTING, M.D.\*

BOSTON

## EFFECT OF FLUORINE ON DENTAL CARIES

THE earliest references in the literature on the relation of fluorine to dental caries were made in 1916 by McKay and Black,<sup>56-57</sup> who studied the so-called "Colorado brown stain." During the following decade mottled enamel and dental caries were extensively studied by McKay<sup>58-59</sup> and Bunting et al.<sup>61</sup> It was not until 1931, however, according to Dean<sup>60</sup> that fluorine was discovered as the cause of mottled enamel. Four methods were used in studying the cause, prevalence and control of mottled enamel and the lowered prevalence of dental caries in certain areas. These consisted in refinements in measuring the rates of prevalence of caries in relation to age, sex and race<sup>61</sup>, elimination of the circulation factor, or limitation of observations to persons continuously exposed to the specific environment factor under investigation — the common water supply<sup>62</sup>, the development of a chemical method permitting water analyses that were accurate to 0.1 part per million of fluorine<sup>63</sup>, and the development of quantitative methods for estimating the number of *Lactobacillus acidophilus* in saliva, this being used as an index of the activity of dental caries.<sup>64</sup>

The role of fluorine in dental health is ably described in a monograph entitled *Fluorine and Dental Health*, a publication of the American Association for the Advancement of Science edited by Moulton.<sup>65</sup> Another important monograph, entitled *Fluorine in Dental Public Health*,<sup>66</sup> is the report of a symposium at the ninety-fourth monthly conference of the New York Institute of Clinical Oral Pathology, held in New York City in 1944. Finally, by resolve of the General Court, the Massachusetts Department of Public Health<sup>67</sup> prepared in 1945 a monograph entitled *Special Report Relative to the Decay of Teeth Resulting from a Lack of Fluorine*.

## Mottled Enamel

Following the original work of McKay<sup>68</sup> in discovering the condition now called mottled enamel, surveys were made in other communities in which discolored teeth were prevalent.<sup>69</sup> The relation of mottled enamel to water supplies from deep wells had been established as long ago as 1918 by the same author,<sup>69</sup> but it was not until 1932 that the

fluorine content of water supplies was related to this condition.<sup>70</sup> In 1928, the United States Public Health Service undertook to investigate mottled enamel and deformity of teeth of children at Bauxite, Arkansas. The Aluminum Company of America,<sup>71</sup> which owned a mine near which the town was located, caused samples of water to be examined in its laboratory. This examination disclosed that the water from the deep wells supplying the town contained an unusually high content of fluorine. Soon similar findings revealed that a water supply of a high fluorine content was a common factor among children who had developed mottled enamel. Examination of water supplies in communities in which no mottling was found revealed that fluorine was present in extremely small quantities, less than two parts per million.

It was recommended that Bauxite obtain a water supply that did not contain fluorine, and this was done. In 1938, ten years after the town had begun taking water from the Saline River, which contained practically no fluorine, Dean<sup>74</sup> and others<sup>75</sup> reported that all children who had used the water from the deep wells during infancy and early childhood showed mottled enamel. On the other hand, the same children exhibited a low incidence of dental caries, even though they had been using fluorine-free water for twelve years. In contrast, children living in the nearby town of Benton, who had used Saline River water throughout their lifetime, showed no mottling of enamel but a high prevalence of dental caries. Other evidences of the beneficial effects of fluorine were also found. Children of Bauxite who were born within a few years after the change in water supply and had therefore used the old water for only three or four years showed practically no mottling but had a low incidence of dental caries. The children born after the new water supply was obtained showed the highest caries index. Similarly, mottled enamel has been eliminated at Oakley, Idaho, and Andover, South Dakota, by changing the water supply from one containing amounts of fluorides toxic to calcifying dental enamel to one with a fluoride content not

\*Numerous attempts<sup>72,73</sup> have been made to remove excess fluorine from water supplies by using tricalcium phosphate, magnesium oxide or magnesium hydroxide. Of these chemicals, magnesium oxide is the least expensive. The commercial light grade is better than the commercial calcined one, but its higher cost is not in proportion to its greater efficiency. It may be stated that whenever possible it is better to obtain a new water supply containing only 1 p.p.m. (part per million) of fluorine than to attempt defluorination.

\*Commissioner, Massachusetts Department of Public Health and lecturer in public health practice, Harvard School of Public Health.

exceeding 1 p p m.<sup>76</sup> The unusually long interval in time, eight to ten years, before the clinical effects resultant from a change in the water supply may be observed clinically, is unique in epidemiologic investigations of water-borne diseases.

Communities, seeking new water supplies<sup>77</sup> in areas where deep wells are required should have detailed chemical analyses performed before making the new supply available to the public. The city of Narka, Kansas, developed two new deep wells 262 feet deep, the water from these contained 12 and 13 p p m of fluorine, respectively. Epidemiologic investigation of private water supplies from deep wells in the areas surrounding the new wells, however, showed that 8 children who were raised on these private supplies containing 0.8 to 3.0 p p m of fluorine had not developed mottled enamel. Hence, the new supply was made available.

#### FLUORINE-CONTAINING WATER SUPPLIES AND DENTAL CARIES

Meanwhile, other studies had been in progress to determine how much benefit fluorine exerted in the prevention of dental caries. The South Dakota studies made by Dean and McKay<sup>78</sup> in 1938 showed sharp differences in the prevalence of dental caries, depending on whether the population was affected with dental fluorosis. Dean and McKay's article contains a report on the examination of 236 nine-year-old children with a verified continuity of exposure to the fluorine-containing domestic waters of the cities in which they lived. It was noted that there was relative freedom from dental caries in deciduous teeth as well as permanent teeth, whether or not the teeth showed macroscopic evidence of mottled enamel. In 1939, Dean et al.<sup>78</sup> and others<sup>79</sup> reported a study of four cities in Illinois. In Galesburg and Monmouth, where the water contained 1.8 and 1.7 p p m of fluorine, respectively, the children examined showed an average of 2.0 DMF teeth per child. In Macomb and Quincy, where the water supplies contained only 0.2 p p m of fluorine, the children showed an average of 4.0 and 6.3 DMF teeth, respectively.

Another study was made by Dean and others<sup>80</sup> to determine the lowest concentration effective in reducing the incidence of dental caries and the magnitude of this inhibition. Eight suburban cities around Chicago were selected. The water of Elmhurst, Maywood, Aurora and Joliet had 1.8, 1.2, 1.2, and 1.3 p p m of fluorine, respectively. Elgin was intermediate, with 0.5 p p m, and Evanston, Oak Park and Waukegan used fluorine-free water. The prevalence of dental caries in these eight cities, expressed as an average of the number of DMF teeth per child, was as follows: Elmhurst, 2.5, Maywood, 2.6, Aurora, 2.8, Joliet, 3.2, Elgin, 4.4, Evanston, 6.7, Oak Park, 7.2, and Waukegan, 8.1.

It will be seen that children living in the communities using water with the higher fluorine con-

centration had markedly less dental caries than did those living in communities using fluorine-free water, and that 0.5 p p m was not sufficient to give appreciable protection. The populations in these cities were so nearly similar from other points of view that it is difficult to ascribe these differences in the prevalence of dental caries to any other cause than the differences in the concentration of fluorine in the water supply. Moreover, the inhibiting effect was exhibited at such a low concentration that mottled enamel as an esthetic problem was not encountered.

In another study,<sup>81</sup> including examinations of children in twenty-one cities in four states, the level at which the inhibiting factors operate was made even clearer (Table 3). It will be noted that there was a marked drop in the beneficial effect when the concentration was under 0.5 p p m of fluorine, and

TABLE 3 *Relation of the Prevalence of Dental Caries to the Fluorine Content of Water Supplies*

FLUORINE CONCENTRATION OF WATER SUPPLY	NO OF CITIES	NO OF CHILDREN EXAMINED	NO OF PERMANENT TEETH SHOWING DENTAL CARIES PER 100 CHILDREN
p p m			
Less than 0.5	11	3,867	700+
0.5 to 0.9	3	1,140	400+
0.9 to 1.4	4	1,403	300
More than 1.4	3	847	250

that there was no appreciable increase in the inhibiting effect when the concentration was above 1.4 p p m.

The mechanism whereby this element contributes to the prevention of dental decay is thought to be primarily one of increased fluorine content of the tooth enamel.<sup>82</sup> This may result from incorporation of fluorine in the tooth during the period of tooth formation or by acquisition of fluorine from the external surface of the tooth after eruption. There is an affinity between the calcium phosphates of the tooth and fluorine. This fluorine increment in the enamel makes the tooth less soluble in acids. Also, in an environment of fluorine the acid and bacteria in the vicinity of the teeth are reduced. Thus, it seems that at least one substance has been found that successfully counteracts the effects of acids produced by the growth of bacteria in the presence of carbohydrates.

#### ADDITION OF FLUORIDES TO PUBLIC WATER SUPPLIES

Since it has been demonstrated that fluorine found naturally in water supplies combats the inroads of dental caries, one of the first practical questions that arise is whether this useful element can be purposely supplied in areas where it is absent from or extremely low in the water supply. Any domestic water supply, so far as its fluoride content influences dental health, may be thought of as falling into one of three classes — water supplies naturally

with the optimal concentration of fluorine (about 10 p.p.m.), water supplies with an excess of fluorine, requiring its removal to protect the population against endemic dental fluorosis (mottled enamel) or its replacement by or mixture with other water supplies low in fluoride, and water supplies deficient in fluorine, to which it might be added to bring about an optimal concentration of this element so as to lessen the amount of dental decay.

Several states have made detailed analyses of the fluorine content of public and semipublic water supplies. New Jersey has six communities with public water supplies having a fluorine content between 10 and 24 p.p.m. This survey, conducted by Wisan,<sup>52</sup> revealed that children in these communities had a lower caries rate than children living in communities serviced with fluorine-free water. Extensive studies have been made of water supplies in Florida,<sup>53</sup> Illinois,<sup>54</sup> Indiana,<sup>54</sup> Louisiana,<sup>55</sup> Nebraska,<sup>56</sup> New Mexico,<sup>57</sup> North Dakota,<sup>58</sup> Ohio,<sup>59</sup> South Dakota,<sup>60</sup> Texas,<sup>61</sup> Utah,<sup>62</sup> Virginia,<sup>63</sup> and Wisconsin<sup>64</sup> and in 1945 complete mineral-water

presence of fluorine in excess of 15 p.p.m. shall constitute grounds for rejection of the supply.

Massachusetts<sup>67</sup> waters contain extremely small concentrations of fluorine. The maximum quantity found in any one sample was 12 p.p.m. in the semipublic supply at Farnumsville in Grafton. Unfortunately, the number of children who continuously used this supply was too small to justify any conclusions relative to the effect of the fluorine on the caries rate. Fluorine concentrations of 1.0 and 0.7 p.p.m., respectively, were found in deep wells used only as auxiliary water supplies at Lyonsville in Colrain and at Fisherville in Grafton, but the regular water supplies of these communities were low in fluorine. Of 368 samples analyzed, 359 (98 per cent) contained 0.2 p.p.m. or less, and 229 (62 per cent) contained 0.1 p.p.m. or less. The average of all samples was 0.11 p.p.m., an amount that is far below the optimal 1.0 p.p.m. that is effective in lessening dental caries.

Sodium fluoride may be added in correct amounts to a water supply. Ast<sup>68</sup> describes a plan to deter-

TABLE 4 Data on Topical Application of Fluoride

PLACE AND AUTHOR	CHILDREN		NO. OF TREATMENTS PER YEAR	STRENGTH OF FLUORIDE SOLUTION	REDUCTION IN CARIES RATE
	NO.	AGES			
Brockton, Mass. (Bibby <sup>69</sup> )	90	10-13	3	0.1 (NaF)	46
Indiana (Chernus <sup>70</sup> )	46	4-6	2	0.05 (KF)	50
Minnesota (Knutson and Armstrong <sup>71</sup> )	289	7-15	(in 4 mo.) 7-15 (in 8 wk.)	2.0 (NaF)	40
Coast Guard (Arnold et al. <sup>72</sup> )	188	17-22	1	1.0 (NaF— acidulated)	0
Cambridge, Mass. (McKelleget and Bibby <sup>73</sup> )	47	6-14	3	1.0 (NaF)	43
Milville, Mass. (Labunsky and Bibby <sup>74</sup> )	91	6-14	2	1.0 (NaF)	25

analyses were made of all public and semipublic water supplies in Massachusetts.<sup>67</sup> The literature contains many references to the finding of endemic fluorosis in Argentina, Australia, China, Chosen, Ecuador, England, Greenland, India, Malaya, Mexico, Java, South Africa, Tristan da Cunha and Western Asia (Iraq, Trans-Jordan, Syria, the Bahrain Islands, Arabia and Palestine).<sup>65</sup>

The present standard for fluorine content of public water supplies, as defined by the United States Public Health Service, calls for the rejection of the water supply if it contains more than 1.0 p.p.m. The recommended methods of analysis of water supplies are those contained in *Standard Methods for the Examination of Water and Sewage* of the American Public Health Association and a committee report, "Methods of Determining Fluorides," that appeared in 1941 in the *Journal of the American Water Works Association*.<sup>95</sup>

A circular letter from the United States Public Health Service to the Advisory Committee on Drinking Water Standards,<sup>96</sup> on the tentative revision of the 1942 standards, recommends that the

mine the practicability, efficacy and safety of fluorinating a communal water supply deficient in fluorine to control dental caries. Three communities are now conducting such studies—Grand Rapids, Michigan,<sup>97</sup> Newburgh, New York<sup>98</sup> and Marshall, Texas.<sup>99</sup>

#### TOPICAL APPLICATION OF FLUORIDES

Because it was suspected that fluorine could act directly on the teeth through the external surface, one of the first methods of using fluorine was the application of solutions of sodium fluoride directly to the teeth, either in the mixtures used in cleaning the teeth or in simple solutions after such cleaning had been performed by dentists and their assistants.<sup>66</sup> The results of a few of these studies are shown in Table 4.<sup>97</sup>

It will be seen that when these applications are made in children of the youngest age groups, the caries reduction varies from 25 to 50 per cent and that similar applications in adults produce little effect. Undoubtedly, when the proper concentration of solutions and the optimum number of appli-

cations have been determined, one can expect the caries reduction to be regularly over 50 per cent. The principal drawback of this method of the use of fluorine is that it must be carried out in the dentist's office or under the supervision of a dentist, and that the results will be limited by the fact that there are not sufficient dentists and dental assistants<sup>104</sup> available to give treatments to all of the persons in the areas in which the fluorine content of the water supply is low. Other methods of using fluorine must therefore be found to supplement direct applications in the dentist's office. At the present time, studies are in progress in various states to determine whether fluoride added to mouthwashes or dentifrices exerts a beneficial effect.

### *Fluorine in Foods*

The question has been raised whether sufficient amounts of fluorine can be obtained from food materials to exert a beneficial effect. This matter has been investigated by a number of workers<sup>105, 106</sup>. It has been found that most foodstuffs contain extremely small quantities of fluorine. As would be expected, the quantities are somewhat increased in high-fluorine areas, particularly if vegetables are irrigated or sprayed with water containing fluorine. The supply of foodstuffs coming from such areas, however, constitutes such a small portion of the total quantities used that the general level of fluorine is not raised to any significant degree. It has been found that fluorine is excreted in the feces, urine and sweat in sufficient quantities so that the amount obtained from food supplies is lost so promptly that no beneficial effects can be expected<sup>107</sup>. The only food materials with a high quantity of fluorine are those that contain bone or bone meal, such as small fish the bones of which are consumed or baby foods to which bone meal has been added. It has been observed that certain primitive peoples who depend largely on fish for protein show a low attack rate of dental caries. It may be that this is due to the fluorine in the bones of the fish.

Although this field has not been thoroughly explored, it appears likely that persons living in modern American communities will not receive much benefit from fluorine obtained from food supplies. If it is eventually demonstrated that the beneficial effect of fluorine is due to the local contact when water flows over the teeth and not to the fact that fluoride is assimilated by the blood supply, this may further explain why fluorine in foods is not more effective, since it is not so easily available for a local effect, being intimately bound up with the foods.

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It will be seen from the foregoing discussion that all practitioners of the healing arts have good reason to believe that fluorine exerts a direct beneficial effect in preventing dental caries. It may even

be that the higher prevalence of dental defects in New England, as well as elsewhere, can be ascribed to the absence of this useful chemical. If this proves to be the case, the simple addition of fluoride to water supplies or to other materials widely used by the public may exert a profound effect on this public-health problem. It is important, however, that fluorine be used judiciously, because it not only exerts a beneficial effect but if used in excess may have a deleterious effect on the teeth. Care must therefore be employed against supplying the chemical in amounts large enough to produce dental fluorosis.

There are probably many factors that affect the action of fluorine that are yet to be investigated. For instance, it has been noted that in northern India, where the fluorine content of the water supply is high and the general diet is superior, the natives do not develop fluorosis<sup>108</sup>. On the other hand, the condition is frequently seen in southern India, where the diet is much less adequate and the fluorine content of the water is no higher. Susceptibility to fluorosis therefore seems to increase through lack of certain essential nutrients.

### CURRENT RESEARCH ON DENTAL CARIES AND FLUORINE

Further studies are necessary to determine the best methods for utilizing this useful chemical. To learn of any research recently begun or in progress in other states that has not yet been described in public-health and dental journals, letters were sent to all the health officers of the states and provinces of the United States and Canada asking for such details as were available. Attention was called to the fact that the Massachusetts Department of Public Health was particularly interested in research regarding the effect of fluorine. The information obtained is summarized in Table 5, and a short description of the projects in a few of the states follows.

*Alabama* Studies are being conducted in establishing prevalence rates for dental disease. The Department of Geology of the University of Alabama is making a study of the ground-water supply, financed by the State Health Department, to determine the amount of sodium fluoride it contains. State-sponsored clinics will utilize topical applications of sodium fluoride on half of a series of patients, the other half serving as controls. Further work on the use of fluoride in topical applications will be carried on, the state dentist working in collaboration with the Department of Geology of the University of Alabama.

*California* Drs. Becks and Wainwright, of the California Dental College, have carried out studies on the relation of *B. acidophilus* to dental caries. Becks and his co-workers are also studying the effect of fluorides on dental tissues.

*Connecticut* Projects have been set up to show the local effects of fluorides on tooth structures. These include the study of the effect of adding fluoride to the water supply of the Southbury Training School, tooth analyses are being made

*Illinois* Plans are being made for a study of the use of fluoride in the public water supply as a dental decay preventive in Evanston. Previous work has been done by the United States Public Health Service on the relation between dental caries and

TABLE 5 Dental Caries Research Programs in the United States and Canada 1945

STATE OR PROVINCE	SURVEY OF FLUORINE IN WATER SUPPLIES	ADDITION OF FLUORIDE TO DRINKING WATER	OTHER FLUORIDE STUDIES (TOPICAL APPLICATION, ETC.)	OTHER DENTAL-CARIES STUDIES
Alabama	In progress	—	Planned	Prevalence rates
Arizona	—	—	—	—
California	—	—	In progress	Bacterial counts
Connecticut	In progress	In progress	In progress	Prevalence rates and bacterial counts
Delaware	—	—	—	—
Florida	—	—	—	Prevalence rates
Georgia	—	—	—	Prevalence rates
Idaho	—	—	—	Prevalence rates
Illinois	Completed	Planned	—	Prevalence rates
Indiana	Planned	Planned	Planned	Prevalence rates
Iowa	In progress	—	—	Prevalence rates
Kansas	In progress	—	—	Prevalence rates
Kentucky	—	—	—	—
Louisiana	—	—	—	—
Maine	Completed	—	—	Prevalence rates
Maryland	Planned	—	In progress	Planned
Massachusetts	Completed	Planned	In progress	Prevalence and incidence rates
Michigan	Completed	In progress	Planned	Prevalence rates
Minnesota	—	—	In progress	Prevalence rates
Mississippi	—	—	In progress	Prevalence rates
Missouri	—	—	—	—
Montana	—	—	—	—
Nebraska	—	—	—	Prevalence rates and bacterial counts
Nevada	Completed	—	—	—
New Hampshire	—	—	In progress	Prevalence rates
New Jersey	—	—	In progress	Prevalence rates etc.
New Mexico	—	—	—	—
New York	Completed	In progress	Planned	Prevalence rates etc.
North Carolina	—	—	—	—
North Dakota	Completed	—	—	—
Ohio	Completed	In progress	In progress	Prevalence rates etc.
Oklahoma	Completed	In progress	In progress	Ammoniacal silver nitrate (topical)
Oregon	Planned	Planned	Planned	Prevalence rates
Pennsylvania	—	—	In progress	Prevalence rates
Rhode Island	—	—	In progress	Prevalence rates
South Carolina	—	—	—	—
South Dakota	Completed	—	—	—
Tennessee	—	—	—	Time and cost studies
Texas	Completed	In progress	—	—
Utah	—	—	—	—
Vermont	—	—	—	Prevalence rates and nutrition
Virginia	—	—	—	—
Washington	Planned	—	—	Prevalence rates and bacterial counts
West Virginia	—	—	Planned	—
Wisconsin	In progress	Planned	In progress	Caries studies (general)
Wyoming	—	—	—	—
Alaska	—	—	—	—
Hawaii	—	—	—	—
Puerto Rico	—	—	—	—
Canada	—	—	—	—
Alberta	In progress	—	—	—
British Columbia	—	—	—	—
Manitoba	In progress	—	—	—
New Brunswick	—	—	—	—
Nova Scotia	—	—	—	—
Ontario	In progress	In progress	—	Incidence rate and bacterial counts
Prince Edward Island	—	—	—	—
Quebec	—	—	—	—
Saskatchewan	—	—	—	—

and *B. acidophilus* counts recorded. Topical applications of fluoride are being studied at the County Temporary Home for Children. The effects of a mouthwash containing 5 p.p.m. of sodium fluoride are being examined.

*Georgia* Preliminary studies are being made by Dr. Dean, of the United States Public Health Service, in an area low in caries prevalence to ascertain the basis for the low attack rate and its relation to the concentration of fluoride in the water supply.

the fluoride content of the local water supplies in several cities.

*Iowa* During the last three years there were conducted oral examinations of 12,000 high-school pupils in areas with water supplies high and low in fluoride. The average DMF rate per 100 children in the high areas was 200 to 300, that in the low areas ranged from 300 to 600.

*Kansas* Surveys have been conducted of the distribution of fluoride in city water supplies and the DMF rates of children in the eastern third

and the western third of the state. High rates were found in low-fluorine areas.

**Maine** An investigation of the incidence of caries was conducted for a number of years, and a study of the analysis of drinking water was made.

**Maryland** A prewar investigation of fluorine in water supplies was begun by the United States Public Health Service but has been delayed until more personnel is added. A statistical study of caries was made.

**Massachusetts** Study of the effect of fluorine on decay of the teeth has been authorized by the Legislature, with a small appropriation. Some studies on fluorine had already been begun by the Tufts College Dental School and the Massachusetts Department of Public Health. Surveys of the prevalence of dental caries are in progress. The fluorine content of all public water supplies has been determined. These activities are to be extended with the expansion of dental personnel and formation of a division of dental health.

**Michigan** The Department of Public Health and the United States Public Health Service are conducting a pilot program in the utilization of 1 p.p.m. of sodium fluoride in the public water supply of Grand Rapids as a preventive of dental caries. Other projects are being carried on in the field of fluoride therapy and diet at the University of Michigan Dental School.

**Minnesota** A pilot study is being made by Dr. Knutson, of the United States Public Health Service, on the topical application in a 2 per cent solution of sodium fluoride in 289 school children. Three other studies are being carried on along the same lines by the Department of Public Health in the towns of Hibbing, Chisholm and Virginia.

**Mississippi** Preliminary studies are being carried on by Dr. Hagan, of the United States Public Health Service, in two counties on the effectiveness of topical applications of sodium fluoride.

**Nebraska** Studies were made on the relation of *B. acidophilus* to dental caries at Boys' Town.

**Nevada** A preliminary study is being made of the production of dental fluorosis by varying high percentages of fluorine in the water supply.

**New Hampshire** Two demonstrations are in progress on the topical application of fluoride to tooth structures.

**New York** The State Department of Health is conducting a pilot program in the utilization of 1 p.p.m. of fluorine in the public water supply of Newburgh. Kingston, across the Hudson River, is used as the control community. Other projects in fluoride therapy are contemplated.

**Ohio** The United States Public Health Service has been conducting a fluorine project in Garrettsville for the last five years. Fluoride has been added to the water supply in this community. A fluorine study is being conducted in Miami

County by the United States Public Health Service, this will include topical applications of sodium fluoride.

**Oklahoma** Investigations are being conducted of the value of ammoniacal silver nitrate precipitated with eugenol as a means of controlling incipient caries. The program is both remedial and preventive.

**Pennsylvania** Two limited programs are being conducted on the topical effects of sodium fluoride.

**Rhode Island** Studies are being initiated in the topical effect of sodium fluoride at the St. Aloysius Orphanage, with the use of a 2 per cent solution of sodium fluoride, and by the Abby Frances Lawton Dental Clinic in Central Falls, under Dr. Bibby's direction. In West Warwick (20,000 population) there is a projected study of all school children in relation to the attack rate of caries and the introduction of fluorine into the water supply.

**Texas** Marshall is adding 1 p.p.m. of fluorine to the public water supplies. Jacksonville will be used as a control. This is a pilot program.

**Washington** The Washington Department of Health is offering laboratory service to private practitioners for counts of *B. acidophilus* and is making a study of diet in relation to the control of dental caries.

**West Virginia** The West Virginia Department of Public Health has suggested a technic to dentists in the topical application of sodium fluoride.

**Wisconsin** Preliminary surveys were made to determine the prevalence of dental caries. Further work is progressing on a comparison of the incidence of caries among kindergarten children in two cities—Green Bay, with a fluorine content of 2.3 p.p.m. in the water supply, and Sheboygan, with 0.05 p.p.m. Sheboygan proposes to add fluorine to the water supply. Other studies of long duration are contemplated.

**Canada** A study is in progress in Alberta on the relation of mottling of enamel to the low incidence of dental decay. In Ontario, the Department of Health, in co-operation with the Research Department of the Faculty of Dentistry, University of Toronto, is making water analyses and surveys to ascertain the incidence of dental caries. Dental surveys were conducted in two fluorine-free municipalities. Following the survey, one of the municipalities introduced fluoride into the water supply.

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546 State House

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## CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

### Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

#### CASE 32241

##### PRESENTATION OF CASE

A forty-nine-year-old housewife entered the hospital because of cramps in the legs and carpopedal spasm.

The patient had apparently been well until three days before entry, when she noticed cramps in the calves of both legs, which gradually increased in severity. She also became nauseated, vomiting several times. The following day the vomiting became worse, and she took bicarbonate of soda, which apparently gave some relief. On the afternoon of admission she first noticed spasms causing the hands to flex sharply. This was accompanied by a sensation of "pins and needles" in the arm muscles but no pain.

The patient had passed a total of only 500 cc. of urine since the onset of her illness, although she had frequency of six or seven times a day and two or three times a night. A urinalysis by a local doctor on the day before entry had shown the urine to be heavy in albumin. The last adequate urine output was four days before entry. There was no history of any other urinary symptoms, although her husband stated that during the previous nine months she had occasionally complained of pain in the left groin and flank. There had been no chronic illness, weight loss, headache, stiff neck or food poisoning. The only drugs she recalled taking recently were stilbestrol, occasional small amounts of phenobarbital, aspirin and Karoid with bile salts.

In the past her health had always been excellent. Her two pregnancies were uncomplicated. She was treated at this hospital for a fistula-in-ano nine years before entry, when the urine showed a ++ test for albumin, with 150 white cells per high-power field, and a specific gravity of 1.026. A year later the specific gravity was 1.027, with eight white cells per high-power field and a + test for albumin. The fistula healed satisfactorily.

Physical examination revealed a flushed, drowsy, moderately obese woman who lay quietly in bed but appeared to be in considerable discomfort. She

breathed slowly and quietly. The heart, lungs, and abdomen were normal. The hands showed carpopedal spasm. The calves were tender to compression. There was a strikingly active Chvostek sign. The tendon reflexes were somewhat hyperactive. There was no uremic odor to the breath and no peripheral edema.

The temperature, pulse and respirations were normal, the blood pressure was 135 systolic, 85 diastolic.

Examination of the blood revealed a hemoglobin of 12 gm and hematocrit of 39. The white-cell count was 5200. The nonprotein nitrogen was 136 mg per 100 cc, rising to 145 mg the next day. The serum sodium was 136 milliequiv per liter, the chloride 85 milliequiv, the cholesterol 121 mg per 100 cc, the carbon dioxide content 27.7 milliequiv per liter, the alkaline phosphatase 2 Bodansky units, the phosphorus 9 mg per 100 cc, the calcium 5 mg and the serum protein 5.4 gm. A catheterized urine specimen (only a few cubic centimeters) was amber colored and clear, with a pH of 5.5. There was a +++ test for albumin. The sediment contained rare red cells, 75 white cells, a moderate number of epithelial cells and many granular casts per high-power field. The Sulzowitch test for urinary calcium was positive, and a stool examination was guaiac negative. Repeated urine cultures showed moderate to abundant growth of *Staphylococcus albus*.

A cystoscopy and right retrograde pyelography were negative. An x-ray examination of the chest and abdomen was negative.

The patient appeared markedly improved after intravenous calcium gluconate but despite intravenous saline and glucose failed to pass more than a few cubic centimeters of urine at a time. After cystoscopy the urine became grossly bloody. Penicillin effected no improvement. The nonprotein nitrogen continued to rise, reaching 225 mg per 100 cc on the fifth hospital day, when peritoneal lavage with a solution of glucose, sodium chloride, sodium lactate and gelatin was instituted at the rate of about thirty liters a day. By the eighth hospital day the nonprotein nitrogen had dropped to 115 mg per 100 cc, but the temperature began to rise, and the patient developed a cough productive of small amounts of tenacious mucus. On the tenth hospital day she became disoriented and restless, and the temperature spiked to 105°F. On the ninth hospital day the abdomen was found to be distended and tender, although not particularly rigid. A few rhonchi were heard at the lung bases, and there was a pericardial friction rub. The blood pressure had dropped to 60 systolic, 35 diastolic. Abundant colon bacilli and nonhemolytic streptococci were grown from the peritoneal lavage fluid. The nonprotein nitrogen was 78 mg per 100 cc. Despite continued administration of penicillin, the patient died on the eleventh hospital day.



## DIFFERENTIAL DIAGNOSIS

DR. BERNARD JACOBSON May we see the films of the pyelogram?

DR. TRACY B. MALLORY There is no roentgenologist here, but Dr. Lingley reports that the films are entirely negative.

DR. JACOBSON To me, at least, one of the most disappointing findings in this case is the normal pyelogram. It upsets a good many possibilities that I should like to entertain. There is no evidence of any postrenal obstruction. I assume that the findings on the left side would have been similar had a left retrograde pyelogram been done. It looks like a good x-ray film to me. Do you agree, Dr. Colby?

DR. FLETCHER COLBY We did not do a bilateral pyelogram because the patient was in a precarious state at that time. We were interested in demonstrating, if we could, the presence of at least one normal kidney, which we succeeded in doing. This pyelogram was interpreted as being entirely normal.

DR. ALLAN M. BUTLER The history mentions pain in the left groin and flank. In view of the history I should like to know why a right pyelogram was done.

DR. COLBY At that time I did not know of the pain in the left groin and flank.

DR. JACOBSON To go back to the case, it is of interest that the duration of the whole illness prior to entry was three or four days after the onset of clinical tetany and oliguria. There is no question that the patient had some type of renal insufficiency with other complications later. This certainly is not an orthodox case of diffuse renal failure. There are many things lacking for a positive diagnosis of terminal chronic glomerulonephritis or chronic vascular nephritis, such as the absence of history of previous acute or chronic vascular renal disease. The patient had normal blood pressure. Many usual symptoms of uremia were absent. It is significant that she had a normal carbon dioxide content of the blood and no clinical or chemical evidence of acidosis. It is also important that she had a normal fixed base, a normal sodium in the blood, which is not an ordinary finding in uremia due to diffuse renal disease.

The first thing that struck me as unusual, regardless of the cause of renal insufficiency, was the presence of marked tetany in association with an extremely low blood calcium and extremely high blood phosphorus. This is a combination that I have never seen in renal insufficiency. It is true that the serum calcium sometimes falls slightly in ordinary renal failure, it may fall to 9.0, 8.5 or 8.0 mg per 100 cc. I have never seen it fall in renal failure to a tetanic level. The rise of the phosphorus, of course, can be entirely due to phosphorus retention by insufficient kidneys. On the other hand the presence of a positive Sulkowitch test, which means an excess of calcium excretion in the urine, is a

stumbling block in trying to explain the whole metabolic set-up. With a mild degree of hypocalcemia, of chronic terminal nephritis, the calcium excretion is either unchanged or is lowered as pointed out by Albright and Bauer<sup>1</sup> many years ago. Could this degree of hypocalcemia be related to the lowering of the serum protein? In cases of renal insufficiency accompanied by mild hypocalcemia, it is thought that the depression is due to or related to the slight depression of serum protein, but in this particular case the lowering to 5.2 gm does not seem adequate to explain the marked hypocalcemia. I should estimate with this degree of hypoproteinemia that the calcium might otherwise be lowered to approximately 8.5 mg, calculating about 2.0 mg attached to protein. So far as I can see there is only one known entity in which this type of calcium and phosphorus and clinical tetany can fit properly, and that is hypoparathyroidism. On the other hand, the positive Sulkowitch test is against that diagnosis, because in real hypoparathyroidism, with tetany, the calcium excretion in the urine goes down very markedly. I think the degree of hypocalcemia and the tetany make it likely that this patient had hypoparathyroidism rather than the hypocalcemia of renal failure.

The onset of oliguria suggests that renal insufficiency, with deficiency of renal secretion, had occurred, and it is worth while to consider the various causes of failure of renal secretion. Defective renal secretion is often seen in clinical shock and in conditions of severe dehydration, that is, prerenal failure, when there is not enough blood circulating to the kidneys to secrete urine. There is no evidence of postrenal failure. No lesion in the ureters or pelves that is obstructing the outflow of urine can be demonstrated.

What are the possible intrinsic renal causes of failure of renal secretion? The most frequent cause is some type of tubular obstruction or, in these days, poisoning from the administration of sulfonamides. Poisoning of the tubules with mercury can produce a somewhat similar picture. There is no evidence that the patient had an incompatible transfusion, with the precipitation of hemoglobin in the tubules, or that she had precipitated Bence-Jones protein in the tubules. We are told that so far as could be ascertained the patient had recently taken some stilbestrol, phenobarbital, aspirin, and Karoid with bile salts. So far as I know there is nothing in these drugs to produce tubular obstruction. In view of the fact that she had had some urinary-tract infection over a period of years one wonders whether she had not been given sulfadiazine or sulfathiazole prior to the onset of this illness. We have no evidence of sulfonamide administration in this case.

We must boil down this type of renal failure to something. Could this possibly be the terminal stage of chronic pyelonephritis? There are many

things against and a few things suggestive of this possibility. Against the diagnosis is the fact that this woman had been well, with no long history of symptomatic urinary-tract infection. On the other hand we know that at least nine years previously she had a moderate amount of urinary-tract infection. I suspect that at that time the urinary findings with high-specific gravity of 1.026 represented cystitis. There is no evidence of an infectious renal lesion, such as tuberculosis, or, at the time of entry, of generalized sepsis that might have terminated in multiple renal abscesses. Against the diagnosis of chronic pyelonephritis is the normal pyelogram and, possibly, the absence of leukocytosis. For the diagnosis of pyelonephritis, however, we have three points: at least nine years previously she was known to have a urinary-tract infection, for about nine months prior to entry she was said to have some pain in the left flank, and finally, the urinary sediment at the time of admission consisted mainly of white cells and granular casts consistent with the picture of pyelonephritis. We are told that the one small specimen of urine observed was amber in color. That would suggest a specific gravity much higher than that found in secondary renal failure.

This patient undoubtedly died partly because of a complication of the treatment. Most of us have read a fairly recent clinical report in the *Journal of the American Medical Association* by Fine et al.<sup>2</sup> on the removal of nitrogenous bodies in the blood by lavage of the peritoneal cavity, using the peritoneal cavity as a dialyzing membrane. That was obviously attempted in this case. That dialysis did something is evidenced by the fact that the blood nonprotein nitrogen dropped considerably. The patient did not die with the clinical picture of uremia. On the other hand the increasing abdominal distention and tenderness certainly suggest the onset of generalized peritonitis, and later we are told that colon bacilli and nonhemolytic streptococci were grown from the lavage fluid.

She had some type of pulmonary complication terminally, probably bronchopneumonia, and undoubtedly had generalized sepsis terminally. I have mentioned many of the stumbling blocks that I have tried to circumvent, and I am afraid I am forced to forget one thing: the positive Sulkowitch test, which does not agree with anything. It is possible that calcium or milk was administered shortly before the urine was tested for calcium. For want of a better diagnosis I shall rest on the following: idiopathic hypoparathyroidism, pyelonephritis (*Staphylococcus albus*), generalized peritonitis, bronchopneumonia and terminal pericarditis.

DR MALLORY: Would anyone like to ask any questions of Dr Jacobson, or does anyone wish to suggest any other diagnosis?

DR JACOB LERMAN: I recall a patient who had a diffuse pyelonephritis with tetany and another

several years back, and I am sure that in Dr Albright's series we could find several other examples.

DR BUTLER: I do not see how Dr Jacobson can entertain the diagnosis of hypoparathyroidism in this case with a nonprotein nitrogen of 136 mg per 100 cc, going up to 225 mg, unless the patient when she came in was extremely dehydrated and the degree of dehydration overlooked. The statement is made that she was moderately obese, and obesity often obscures dehydration. What evidence have we concerning the degree of dehydration that resulted from this woman's vomiting prior to entry?

DR CHARLES BURNETT: She was not particularly dehydrated on entry.

DR JACOBSON: May I ask Dr Butler if he believes that the degree of abnormality of calcium and phosphorus in the blood is compatible with nothing but renal insufficiency?

DR BUTLER: I think that is compatible with renal insufficiency. It is not unusual to find a serum calcium of 5.0 mg per 100 cc with a serum protein of 5.4 gm, and an inorganic phosphorus of 9.0 mg in a patient with marked renal insufficiency and elevated nonprotein nitrogen. Unless the patient was severely dehydrated I do not see how the elevation of the serum nonprotein nitrogen could be compatible with hypoparathyroidism.

DR JACOBSON: I do not believe that such a degree of hypocalcemia in uremia is usual in adults.

DR BUTLER: I have seen at least six patients on the adult wards of this hospital with this degree of hypocalcemia in uremia. I am still puzzled about the retrograde cystoscopic examination, puzzled in two respects. First, here is a patient who was having frequency rather than polyuria. Until we got the cystoscopic examination we suspected that a patient of this age with frequency and a history of renal infection might have cystitis but the cystoscopic examination was against it.

DR COLBY: She had no evidence of cystitis from the examination of the bladder.

DR BUTLER: In the hypocalcemia of hypoparathyroidism one gets bladder retention, not frequency. There was a history of frequency and not of bladder retention, which I think is against the hypocalcemia of hypoparathyroidism.

The second thing in the retrograde pyelogram that bothers me is why, if one subjected the left ureter to the trauma of putting a catheter up, one was too timid to inject a little dye to see what the left pelvis looked like. That was the kidney concerning which there was a history of pain.

DR COLBY: Perhaps we were timid about this. On the other hand simultaneous injection of dye to both kidneys has been found dangerous. This woman was passing a small trickle of urine, and I suppose we believed that if we did a bilateral pyelogram and the trickle completely stopped we should think that there was a possibility of having caused complete anuria by this procedure.

DR. MALLORY Dr. Burnett, will you give us the clinicians' impression on the ward about this patient?

DR. BURNETT After repeated questioning we believed that we had ruled out any toxic substance. There was no history of the taking of mercury. We also considered sulfonamides, and repeated questioning during life gave no leads whatever. Our opinion at the time of death was that we were dealing with a bilateral nephrosis of the kidneys. We simply did not know why she had an acute renal shutdown. Subsequent to death we got an additional history that some time during the winter before admission the patient took 6 or 8 gm. of a sulfonamide, probably sulfadiazine. There was a considerable amount of the drug around the house that the family took from time to time, although there was no definite history that she took it before her illness.

### CLINICAL DIAGNOSIS

Acute uremia due to idiopathic renal disease

### DR. JACOBSON'S DIAGNOSES

Idiopathic hypoparathyroidism  
Pyelonephritis (*Staphylococcus albus*)  
Generalized peritonitis  
Bronchopneumonia  
Terminal pericarditis

### ANATOMICAL DIAGNOSES

Sulfonamide nephrosis.  
General peritonitis.

### PATHOLOGICAL DISCUSSION

DR. MALLORY The autopsy, unfortunately, was limited to the examination of the kidneys. We cannot tell you anything about the parathyroid glands. At autopsy the kidneys looked remarkably normal for a woman who had been totally anuric for two weeks. On cutting frozen sections, however, it became evident that all the lower nephron segments were filled with pigmented casts, that there was interstitial inflammation and that there were crystals in some of the tubules that closely resembled sulfonamide crystals. To check the last point, a portion of one kidney was sent to the Chemistry Laboratory, and the material was identified as sulfadiazine. In spite of the negative history we thus have proof that she had ingested some amount of sulfadiazine. The other ordinary causes of lower-nephron nephrosis are absent in this case. There was no blood transfusion, no history of any state of shock, and no extreme dehydration. We know that sulfonamides can produce this lesion. The logical conclusion is that we consider this sulfonamide nephrosis, presumably due to an abnormal sensitivity of this particular patient to the drug.

DR. JACOBSON Was there peritonitis?

DR. MALLORY The immediate cause of death was peritonitis.

DR. JACOBSON How do you explain the normal carbon dioxide content, Dr. Butler?

DR. BUTLER I think it can be explained by the fact that she had been vomiting prior to coming to the hospital and had been taking alkalis. Without the vomiting and without the alkalis the anuria would have been accompanied by acidosis. She came in with a low serum chloride and normal carbon dioxide content, because of the coincidental vomiting and ingestion of alkali.

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### CASE 32242

### PRESENTATION OF CASE

A sixty-year-old man entered the hospital because of difficulty in swallowing.

Two years before admission the patient allegedly vomited about two spoonfuls of bright-red blood. Shortly thereafter he noticed difficulty in swallowing meat, which "got down to the stomach and came right up again." Over a period of a year and a half the difficulty progressed to include all solid foods and then semisolid food until six months before admission, when it became impossible for him to swallow anything but fluids. His diet consisted of ice cream, milk, soup, eggnog, beer and whiskey. The last two items had been a dietary staple for many years, with an estimated daily intake of three or four glasses of whiskey and several glasses of beer. With this illness the patient lost 25 to 35 pounds. He felt weak and hungry, but had no pain or recurrence of hematemesis. The stools had never been black.

Physical examination revealed a thin, pale man, whose skin was hanging in loose folds in many areas. The tongue was coated with caked brown material. The abdomen was soft and flabby. The liver edge extended 5 cm. below the rib margin and was not tender. There were external hemorrhoids. The prostate was small and tender.

The temperature was 98.6°F, the pulse 70, and the respirations 20. The blood pressure was 110 systolic, 75 diastolic.

The red-cell count was 4,030,000, with 12.5 gm. of hemoglobin. The white-cell count was 7800, with 80 per cent neutrophils. The urine had a specific

gravity of 1.014, and the sediment contained 4 white cells and 2 red cells per high-power field. A stool was guaiac negative.

X-ray examination of the esophagus showed an area of constriction at the level of the tenth thoracic vertebra. A hiatus hernia of moderate size was present. The junction between the esophagus and the hernia was markedly constricted, and one area strongly suggested an ulcer crater (Fig. 1). The stomach was normal, but the duodenal cap was deformed. No definite crater was demonstrated. In the chest film the lung fields were bright. The heart was normal in size.

The prothrombin time was 27 seconds (normal, 21 to 25 seconds). The total serum protein was 7.7 gm. per 100 cc, with 5.3 gm. of albumin and 2.4 gm. of globulin. The van den Bergh reaction was normal,



FIGURE 1

but the cephalin-flocculation test was + at twenty-four hours and +++ at forty-eight hours. The nonprotein nitrogen was 26 mg. per 100 cc.

An operation was performed on the thirteenth hospital day.

## DIFFERENTIAL DIAGNOSIS

**DR. EDWARD B. BENEDICT** When any man of sixty comes in with difficulty in swallowing, we ought first to consider carcinoma of the esophagus. This patient is within the age group. On the other hand, two years' duration is a little long, although I have seen carcinoma of that duration.

The vomiting of blood goes with carcinoma, benign stricture, esophageal ulcer or esophagitis. Benign stricture is the second thing I should consider in a patient who has difficulty in swallowing.

Patients cannot always tell how far a piece of food goes down, but it is fairly significant if it comes up immediately.

This patient did not have much of a diet, he must have been malnourished. Beer and whiskey may be taken by a patient with either carcinoma or benign stricture, but I must say that excessive use of alcohol may lead to an esophagitis and possibly esophageal ulcer and stricture.

The weight loss does not help. One can lose weight from carcinoma or esophageal obstruction from low intake of food. Pain is more likely in esophagitis and ulcer than in cancer of the esophagus; in cancer, pain appears rather late.

The enlarged liver makes me think of either metastatic cancer or cirrhosis because of the alcoholic history.

Out of 45 cases of benign stricture of the esophagus that I have looked up, 17 were associated with hiatus hernia, 15 with duodenal ulcer, 8 with esophageal ulcer, and 7 with esophagitis without any of these other factors, which may occur singly or multiply. This patient had hiatus hernia, possibly with esophageal ulcer and evidence of old duodenal ulcer, all of which are consistent with a benign stricture. May we see the x-ray films?

**DR. JAMES R. LINGLEY** I think that the spot films demonstrate the area in the esophagus best. This is the area of narrowing and the esophagus above this point is dilated. The margin comes down to a small taper rather than a shelf. Below the area of constriction one can see gastric mucosa. Evidently the hiatus hernia extends well up to the area of narrowing. On two of the films there is slight pooling of barium at this point, which is consistent with superficial ulceration, although that is not too definite. This is the deformity of the duodenum, there is gross deformity and constriction at the apex of the cap, without a definite crater.

**DR. BENEDICT** You do not see any suggestion of a shelf at that point either?

**DR. LINGLEY** No, it is a smooth, tapering shadow.

**DR. BENEDICT** All the laboratory findings were within normal limits. The cephalin-flocculation test was + at twenty-four hours, which means very little, and +++ at forty-eight hours, which is not sig-

nificant either. So far as liver damage is concerned, none of the tests indicate whether we are dealing with cirrhosis or metastatic cancer of the liver, if either.

I should hope that the operation performed was an esophagoscopy, which is the first thing to do, not only for positive diagnosis by biopsy but also for treatment by bougienage if a benign stricture is found. The treatment of benign stricture of the esophagus by esophagoscopy and bougienage is unusually satisfactory. I saw a recent case of esophageal obstruction with carcinoma of the esophagus and a large liver, which we thought was metastatic carcinoma of the liver and which proved on peritoneoscopy to be cirrhosis. If this case was carcinoma of the esophagus, which I do not think it was, there could have been metastases to the liver. I believe that it was a benign stricture of the esophagus, and the patient may have had early cirrhosis of the liver. My diagnosis is therefore benign stricture of the esophagus, in association with hiatus hernia, esophageal ulcer and duodenal ulcer, and question of cirrhosis of the liver.

DR. F. DENNETTE ADAMS: Is it not simpler to explain the large liver by malnutrition and the rigid feeling in the abdomen by the fact that the patient was formerly fat and had become extremely thin?

DR. RODOLFO E. HERRERA: As I remember it, Dr. Sweet and I thought that this man had a duodenal ulcer, short esophagus and hiatus-hernia syndrome, so that preoperatively we were quite certain that it was a benign stricture, but because of the question of ulcer of the esophagus and the amount of stenosis, we believed that he probably could be cured more permanently and more quickly if he were operated on than if he had bougienage for a long time. At operation a markedly stenosed short esophagus was found, and as is frequently noted it was difficult to visualize how this condition might have been treated successfully with repeated dilatations alone. The patient had a resection of the lower esophagus and a portion of the cardia and an esophagogastric anastomosis. The patient did extremely well. The postoperative course was uneventful. He was discharged on a six-meal bland diet.

#### CLINICAL DIAGNOSIS

Benign stricture of esophagus

#### DR. BENEDICT'S DIAGNOSES

Benign stricture of esophagus

Hiatus hernia

Esophageal ulcer

Duodenal ulcer

Cirrhosis of liver?

#### ANATOMICAL DIAGNOSIS

Benign stricture of esophagus

#### PATHOLOGICAL DISCUSSION

DR. TRACY F. MALLORY: The specimen from this patient consisted of 6 cm. of esophagus in addition to a cuff from the cardia of the stomach. At about the mid-portion of the esophageal segment, there was a short constriction 6 mm. in length where the lumen was reduced to a bare  $\frac{1}{4}$  mm. in diameter. The mucosa was smooth and not ulcerated at any point. The sections through the area of constriction showed only nonspecific inflammatory reaction and fibrosis, an entirely benign lesion. There was nothing in the section that would give one any indication of the cause of the stricture.

DR. RICHARD H. SWEET: Was there any evidence of gastric mucosa?

DR. MALLORY: Not in this case.

DR. HERRERA: I have seen this patient once in the Out-Patient Department. Six months after operation he is back to his old diet, including whiskey and beer, and has told me that he has begun again to have some difficulty in swallowing large pieces of solid food. He was referred to the diet kitchen for a six-meal bland diet, to the X-ray department for further study and to Dr. Benedict for esophagoscopy.

Dr. Sweet might like to comment on the few cases we have seen of gastrointestinal symptoms following resection of the esophagus for inflammatory disease.

DR. SWEET: As Dr. Benedict has pointed out, a short esophagus with ulcer, inflammatory changes and stricture is frequently associated with a hiatus hernia and a duodenal ulcer. The short esophagus and the hiatus hernia I believe to be congenital. There is a difference of opinion regarding etiology. I can never see how an inflammatory stricture, which is often confined only to a short length up and down the esophagus, can pull the cardia 10 or 12 cm. out of the abdomen into the chest. Some of the cardias are as high as the inferior pulmonary vein. I do not know why we hurried over the esophagoscopy at this time unless it was that Dr. Benedict was not here. We have had cases in which the hazards of esophagoscopy were considerable, and I might have decided in his absence not to do it. I am not quite prepared to make a definite statement about this, but I have the distinct impression that there is a high incidence of carcinoma in cases of short esophagus. I shall say it this way: a large number of our cases of carcinoma at the lower end of the esophagus have been seen with this anatomical stricture. In one of Dr. McKittrick's patients on whom he asked me to operate, around the corner at the lower end of the gastric side, far beyond the reach of any instrument, there was in addition to this inflammatory stricture a carcinoma as large as a cherry. It is an interesting group of cases. Another point is that I agree with Dr. Bene-

dict that in all these cases bougienage should be attempted if carcinoma can be excluded. We have not always been able to carry out bougienage. I remember one patient who was transferred to the psychiatric ward because when his wife came to visit him his swallowing difficulty was worse. He ended up with carcinoma and, after we had watched him on the wards for a number of months, was completely inoperable. It did not do him any good to be on the psychiatric ward. We must be extremely careful, and I prefer to err on the side of being radical in some of these cases.

As Dr. Herrera mentioned we have had one or two patients who have had recurrence of esophagitis following resection, possibly because we did not resect enough or possibly because of some inherent

tendency to develop esophagitis. We have another patient in the Baker Memorial Hospital whose esophagus Dr. Benedict is in the process of dilating following resection of an area of esophagitis with stricture. It is a condition that must be studied and worked on a great deal longer before the best methods of treatment are fully established.

DR. BENJAMIN CASTLEMAN: Do you ever see a peptic ulcer due to regurgitation of acid into the esophagus following resection of the lower esophagus?

DR. SWEET: We have seen one in a patient who had a gastrostomy.

DR. BENEDICT: That is the one I have just treated by esophagoscopy and bougienage.

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## ONE HUNDRED AND SIXTY-FIFTH ANNIVERSARY

THE one hundred and sixty-fifth anniversary of the Massachusetts Medical Society, held at the Hotel Statler, Boston, was a fitting celebration of the postwar resumption of the more or less normal activities of the Society. The total registration—1750—established an all-time high, which is surprising in view of the fact that many fellows, as well as many recent graduates who have postponed joining the Society, are still serving with the armed forces.

The annual meeting of the Council was presided over by the retiring president, Dr. Reginald Fitz, with his customary expertness. There were few controversial matters, and all recommendations by

standing and special committees, which at times had been amended by the Executive Committee, were adopted. The report of the Committee on Medical Education, which had been instructed to make a survey of the medical educational facilities available in New England, was of particular interest. Based on a factual study of correlated material from many sources, it was concluded that New England, at the moment, does not need a new medical school and that its present schools can meet the anticipated requirements for the next several years. The increasing activities of the Society were responsible for a request for an extraordinary appropriation to cover the cost of additional secretarial help, which was granted, by the Council. The officers elected for the current year are as follows: president, Dwight O'Hara, president-elect, Edward P. Bagge, vice-president, Isaac S. F. Dodd, secretary, Michael A. Tighe, treasurer, Eliot Hubbard, Jr.; assistant treasurer, Norman A. Welch, and orator, Leland S. McKittrick.

At the annual meeting of the Society, Dr. Fitz gave an excellent talk covering what had transpired during his year of office. After presentation of the incoming president and president-elect, Dr. Frank H. Lahey delivered the annual oration, which will appear in the June 20 issue of the *Journal*.

The annual dinner was attended by approximately 525 fellows and guests. The speakers, Dr. Roger I. Lee and Dr. Elmer S. Bagnall, ably discussed many matters that are of general interest to the medical profession, particularly those having to do with the health of the Nation.

The scientific sessions comprised many well conceived and well presented papers. The Shattuck Lecture was presented by Dr. John B. Youmans, professor of medicine, Vanderbilt University School of Medicine, and formerly colonel, M.C., A.U.S., and chief, Nutrition Branch, Office of the Surgeon General. This paper, entitled, "Nutrition and the War," appears elsewhere in this issue of the *Journal*.

The luncheon meetings of the sections were extremely well attended, as were both the scientific and the technical exhibits, which were excellent. Indeed, many of the exhibitors were enthusiastic over the number of fellows who had visited their booths.

Much of the success of the meeting is due to the diligence and efforts of Dr Roy J Heffernan and his committee and of Robert St B Boyd, the executive secretary. To them the Society should be duly grateful.

## TETANUS PROPHYLAXIS AND TREATMENT

SUFFICIENT time has now elapsed since the termination of the military campaigns to permit a certain amount of stocktaking with respect to the efficacy of some of the procedures used in the medical departments of the armed forces. Brigadier Boyd<sup>1</sup> has now collected and analyzed the cases of tetanus that occurred in the British Army in the African and European theaters of war. His analysis, although based on only 103 cases, brings out many significant features concerning the value and relative importance of active and passive immunization against tetanus.

Boyd points out that the value of the use of prophylactic tetanus antitoxin for passive immunization was adequately demonstrated during World War I. At that time the incidence of clinical tetanus was reduced from a former rate of 8 cases per 1000 wounded to 1 per 1000 among those who received antitoxin within a reasonably short period after sustaining a wound. The average incidence of tetanus among British troops for the years 1914-1918 was 1.47 per 1000 wounded.

In World War II, about 90 per cent of the British troops received prophylactic tetanus toxoid injections. At first, two doses of 1 cc each were given six weeks apart. In January, 1941, the standard procedure was changed to include a third dose, and in November, 1942, an annual booster dose of 1 cc of toxoid came into use. Shortly before the invasion of Europe all members of the army groups received a booster dose. Passive immunity by the injection of 3000 units of antitoxin at weekly intervals for three doses after wounding was recommended for those who had not received active immunization, and a single similar dose was suggested for those who had received toxoid injections. In the United States Army only a booster dose of tetanus toxoid was generally used after wounds had been sustained.

The 103 cases of tetanus included 35 battle casualties, an incidence of 0.14 cases per 1000 casualties. The remaining cases comprised 18 non-battle casualties and 50 partisans and prisoners of war. Of the 35 cases among battle casualties, 16 were in men who, for some reason or other, had escaped active immunization. Indeed, considerable evidence was accumulated, pointing to the fact that clinical tetanus was rare among those who had been actively immunized. For example, among the British Expeditionary Force in Europe during 1939-1940, there were 7 cases of tetanus among the 10 per cent of troops who had not been immunized, whereas not a single case occurred among the 90 per cent who had been given toxoid. In another campaign, there were only 6 cases of tetanus among 103,343 wounded British troops, most of whom presumably had been immunized, whereas there were 25 cases among a small number of wounded prisoners taken during that campaign, none of whom had been actively immunized. As compared with 1.47 cases per 1000 in World War I, there were only 0.06 cases per 1000 in this war, a ratio of almost 25:1.

Further analysis of the possible causes of this marked reduction in incidence of tetanus left little room for doubt that only active immunization was responsible. Evidence was obtained that indicated that the low incidence of tetanus among the British Expeditionary Force in Belgium was not due to any peculiarity in the type of terrain in which the wounds were incurred. Thus, data unearthed in a captured German hospital in Brussels showed that there had been 100 cases of tetanus among unimmunized troops who were wounded in the same terrain in which no cases occurred among the British Expeditionary Forces. Prophylactic treatment with sulfa drugs and penicillin was likewise ruled out as a significant factor.

Several points concerning the effect of active immunization on the severity of the disease and on mortality were also brought out quite clearly from Boyd's study. In the first place, the crude mortality in all the clinical cases during this war was 46.6 per cent, which is practically the same as that observed in 1914-1918, when it was 50 per cent. The mortality was inversely proportional to the length of the incubation period, which reflects a



direct relation to the severity of infection. The case mortality among those who were protected by active immunization was almost identical with that among the unprotected. It is of interest to note, however, that there were no deaths among persons who had received two or more booster doses of toxoid.

Most important, however, was the bearing of previous active immunization with toxoid on the efficacy of passive immunity conferred by the prophylactic injection of antitoxin. Among those who had been actively immunized with toxoid there were 2 deaths in 11 cases (18 per cent) in which prophylactic antitoxin had been given, as compared with 9 deaths in 11 cases (82 per cent) in which such passive immunity had not been used. Among those not actively immunized, there were 10 deaths among 23 patients (44 per cent) who had received prophylactic tetanus antitoxin, and 19 deaths among 39 patients (49 per cent) who had not received antitoxin. In other words, passive protection with antitoxin administered soon after wounding did the most good in the persons who had previously been actively immunized with toxoid.

Pratt,<sup>2</sup> in reviewing the experiences with tetanus at the Children's Hospital in Boston noted that the severity of the disease was the most helpful factor in determining the outcome. As already noted, severity is inversely proportional to the length of the incubation period. In Boyd's study the incubation period in the actively immunized patients was significantly lower than that in those who had not been protected by toxoid. In the protected patients symptoms began in most cases before the tenth day, whereas in most of those who had not been actively immunized with toxoid the incubation period was more than ten days. This appears to indicate that it was necessary to have a much severer disease, in which toxin production occurred at a rapid rate, to break through the residual antibody resulting from the previous toxoid immunization. This breakthrough, moreover, had to take place before the stimulus to renewed antibody production had become effective enough to raise the antitoxin level to a protective value.

The number of cases in Boyd's study was inadequate for an analysis of the value of various therapeutic measures. Early and intensive treat-

ment with antitoxin seemed to be quite valuable. This was suggested by the fact that there were 7 deaths among 18 patients (39 per cent) who received 100,000 or more units within the first thirty-six hours of symptoms, as compared with 14 deaths among 20 patients (70 per cent) not so treated. No additional benefit could be definitely ascribed to penicillin, but this was difficult to assess in the few cases in which it had been used. The same is true in the cases in civilians recently reported by several authors.<sup>3-5</sup>

Boyd concluded that tetanus was not entirely prevented by active immunization, since there were 22 cases among actively immunized persons in his series. Furthermore, the case mortality in actively immunized individuals was not below the average, but he points out that most of the fatal cases occurred among colored troops. The mortality, however, was significantly lower in actively immunized persons who received prophylactic antitoxin. Also the duration of symptoms in actively immunized patients who survived was significantly lowered. Failures of active immunization were attributed to inadequate levels of antitoxin remaining in the blood at the time when the infection took place, and he believes that the best way to remedy this is by the use of prophylactic antitoxin rather than by giving a booster dose of toxoid, as recommended in the United States Army. To be effective in therapy, antitoxin must be given as early as possible, in large doses and intravenously. The experiences of the United States forces have not yet been reported, but there is reason to believe that they were at least as favorable as those of the British in spite of the fact that the use of antitoxin was not encouraged.

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#### MASSACHUSETTS MEDICAL SOCIETY

##### DEATH

ALLEY — Ernest J. Alley, M.D., of Billerica, died May 23. He was in his seventy-second year. Dr. Alley received his degree from the University of Vermont College of Medicine in 1899. His widow and two daughters survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### PSITTACOSIS

Recently a case of psittacosis was reported from the North Metropolitan Health District. Subsequent investigation of the possible sources of this disease led to birds and bird dealers in various sections of the Commonwealth. Inasmuch as the clinical appearance of psittacosis cannot readily be distinguished from that of so-called "virus pneumonia" (of which it is actually one form), there may be more psittacosis in Massachusetts than one suspects.

Birds in the possession of dealers and in private homes, which die of "unknown causes," or diarrhea or any disease characterized by coughing, should be packed in dry ice and sent by air mail to the National Institute of Health, Bethesda, Maryland, for study, with psittacosis in mind.

Samples of serum taken under aseptic precautions from patients who have been in contact with birds and who develop atypical or virus pneumonia should be sent to Dr. Karl F. Meyer, Hooper Foundation, San Francisco, California, for the psittacosis complement-fixation test.

## CORRESPONDENCE

### QUALITY OF MEDICAL CARE

To the Editor: In the April 25 issue of the *Journal* you print an excellent editorial concerning the quality of medical care. You say, in part: "many thousands of graduates of substandard schools are in active practice. Undoubtedly some of these physicians give better medical care than do certain graduates of approved schools." Mere graduation from an approved medical school is no guarantee of an efficient and up-to-date practitioner. You are more than right on both these counts. Many young men go in for medicine because they are forced to by their parents and not because they have any real call to practice medicine. Medicine not being their vocation, they amble through life making weak medical gestures. Some rich persons wish to have a doctor in the family and are willing to pay for the luxury, but the doctor does not amount to much because he does not have the soul of a practitioner. One requires a soul, courage and much more if he essays to succeed in a rural New England practice. Some graduates become so-called "institutional men"; they take salaried hospital jobs, knowing that they would go down swiftly out in the competitive field. Such men would simply dry up and blow away if they did not have a job or private means. They are in no sense practitioners.

Graduation from an unaccredited medical college in no way implies inferiority. It is well known that many of the graduates of the so-called "substandard" medical schools can leave many of their brethren far behind on all counts. It has been said that the top 20 per cent of the poorest medical school are better informed than the lowest 20 per cent of the best medical school. I believe that this statement is unfair to the unaccredited medical schools and that their graduates rank higher. If graduation from small unaccredited medical schools implied inferiority, the world would never have heard of a lot of men whose names are outstanding in the history of medicine and surgery.

In your editorial you speak of a plan in Massachusetts whereby doctors will be admitted to certain privileges in hospitals, such as making rounds, attending clinics and doing other things to improve their education and abilities. This is sound, and I hope that it will come to pass, but as you say yourself some doctors will probably "scorn" to avail themselves of the hospital invitation. Since the American College

of Surgeons has definitely taken the ball away from other big medical associations and has imposed its imperious will on hospitals and countless doctors, the word "scorn" is the correct term. The College has imposed a sort of serfdom on the general run of the profession, something like the *osculum infame* of the ancient European guilds. It will be interesting to see how far they will get with it these days. They have done quite a lot so far, and all in name of "higher standards," "accrediting" or what have you. These terms are a few of the bludgeons held over the hapless heads of many institutions. This has been going on for years, and aside from exterminating a lot of their own brethren, it does not appear that they have accomplished a thing that could not have been done much better in another way. The net result seems to have been the scourging of a lot of hapless physicians and small colleges and hospitals.

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(Notices continued on page xix)

# The New England Journal of Medicine

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Volume 234

JUNE 20 1946

Number 25

## GASTRIC SURGERY\*

FRANK H. LAHEY, M.D.†

BOSTON

SINCE this paper is presented before and will be read largely by physicians interested in the general practice of medicine, in it I will try to cover briefly many of the conditions in which surgery is applicable in the stomach, duodenum and jejunum, and our experiences with them. The latter two structures will be included because their surgical management, either by subtotal gastrectomy or by gastroenterostomy, involves the stomach at the time of the primary surgical procedure and even more seriously involves it when secondary complications, such as gastrojejunal ulcer and gastrojejunocolic fistulas, occur.

### HIATUS HERNIA

If we consider gastric lesions in relation to their anatomic level, and start with the cardia, we can first consider the question of hiatus hernia and, together with hiatus hernia, peptic ulcer of the lower end of the esophagus, which occasionally develops as a result of the hernia.

Hiatus hernia is by no means an uncommon lesion. It is characterized by digestive disturbances and by pain beneath the sternum easily confused with anginal pain. It varies in intensity from acute episodes when good-sized sections of the upper stomach are trapped and distended in the hiatus hernia to the very vague digestive symptoms and very moderate degrees of distress that are associated with small openings through which but small sections of the stomach protrude into the pleural cavity (Figs 1 and 2).

The management of most of these lesions has been successfully accomplished by the Gastroenterological Department of the clinic by medical measures.

Since most of the symptoms associated with hiatus hernia are the result of distention of the herniated portion of the stomach, nonoperative measures are directed largely toward the attainment of more normal digestive function and the avoidance of gastric distention. With the establishment of a careful dietary regimen and the avoidance of laxa-

tives, there have been few of these patients who have but moderate-sized hernias in whom it has not been possible, without surgical interference, to maintain reasonable digestive comfort and to overcome the substernal pain of which most of these patients complain.

We have in the past in a number of these cases attempted to obtain relief by phrenicotomy, but with increased experience in their nonoperative



FIGURE 1 Roentgenogram of a Small Hiatus Hernia Associated with a Congenitally Short Esophagus

management, this procedure has been rarely necessary, and in the cases in which it has been done it has not added significantly to the benefits that can be obtained by medical management alone.

In hiatus hernias with large defects in which good-sized portions of the stomach pass through the

\*The Annual Oration delivered at the annual meeting of the Massachusetts Medical Society Boston May 22 1946

From the Department of Surgery Lahey Clinic

†Director Lahey Clinic

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### PSITTACOSIS

Recently a case of psittacosis was reported from the North Metropolitan Health District. Subsequent investigation of the possible sources of this disease led to birds and bird dealers in various sections of the Commonwealth. Inasmuch as the clinical appearance of psittacosis cannot readily be distinguished from that of so-called "virus pneumonia" (of which it is actually one form), there may be more psittacosis in Massachusetts than one suspects.

Birds in the possession of dealers and in private homes, which die of "unknown causes," or diarrhea or any disease characterized by coughing, should be packed in dry ice and sent by air mail to the National Institute of Health, Bethesda, Maryland, for study, with psittacosis in mind.

Samples of serum taken under aseptic precautions from patients who have been in contact with birds and who develop atypical or virus pneumonia should be sent to Dr. Karl F. Meyer, Hooper Foundation, San Francisco, California, for the psittacosis complement-fixation test.

## CORRESPONDENCE

### QUALITY OF MEDICAL CARE

To the Editor: In the April 25 issue of the *Journal* you print an excellent editorial concerning the quality of medical care. You say, in part: "many thousands of graduates of substandard schools are in active practice. Undoubtedly some of these physicians give better medical care than do certain graduates of approved schools." Mere graduation from an approved medical school is no guarantee of an efficient and up-to-date practitioner. You are more than right on both these counts. Many young men go in for medicine because they are forced to by their parents and not because they have any real call to practice medicine. Medicine not being their vocation, they amble through life making weak medical gestures. Some rich persons wish to have a doctor in the family and are willing to pay for the luxury, but the doctor does not amount to much because he does not have the soul of a practitioner. One requires a soul, courage and much more if he essays to succeed in a rural New England practice. Some graduates become so-called "institutional men"; they take salaried hospital jobs, knowing that they would go down swiftly out in the competitive field. Such men would simply dry up and blow away if they did not have a job or private means. They are in no sense practitioners.

Graduation from an unaccredited medical college in no way implies inferiority. It is well known that many of the graduates of the so-called "substandard" medical schools can leave many of their brethren far behind on all counts. It has been said that the top 20 per cent of the poorest medical school are better informed than the lowest 20 per cent of the best medical school. I believe that this statement is unfair to the unaccredited medical schools and that their graduates rank higher. If graduation from small unaccredited medical schools implied inferiority, the world would never have heard of a lot of men whose names are outstanding in the history of medicine and surgery.

In your editorial you speak of a plan in Massachusetts whereby doctors will be admitted to certain privileges in hospitals, such as making rounds, attending clinics and doing other things to improve their education and abilities. This is sound, and I hope that it will come to pass, but as you say yourself some doctors will probably "scorn" to avail themselves of the hospital invitation. Since the American College

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surgery, have operated on most of these patients, the mortality has progressively diminished until it is now within very reasonable figures

GASTRIC ULCER

The problem of gastric ulcer is one that has occupied the attention of gastroenterologists and surgeons over a great many years, largely owing to the relation between gastric ulcer and gastric cancer

Over the past years we have taken the position that a great many gastric ulcers can be healed and will remain healed under medical management. We have demonstrated this to our satisfaction, and if one could be certain concerning his ability to determine safely which lesion is benign and which lesion is malignant, I should personally be willing to continue with this program. But now, at the end of several years' experience with this position, I believe that it should be changed to the position



FIGURE 4 Preoperative Roentgenogram of a Carcinoma of the Lower End of the Esophagus  
*This was resected transthoracically through the diaphragm, the stomach being pulled up into the chest and anastomosed to the esophagus to make up for the defect*

all carcinomas found at autopsy. Over the years our attitude toward malignant lesions in this location has been so pessimistic that we have not concentrated sufficiently on their early diagnosis. With these lesions now so removable by means of radical surgery, the slightest feeling of discomfort in the lower esophagus, the most trivial degrees of obstruction and the most vague digestive symptoms must be thoroughly investigated with regard to the possibility of this lesion if we are to make full use of the surgical facilities now at hand in attempting to cure a greater number of these patients (Figs 4, 5 and 6)

Mortality figures in these patients submitted to resections of the lower end of the esophagus and upper end of the stomach are shown in Table 1. It is to be noted that, with increasing experience in the hands of Dr. Ralph Adams and Dr. Herbert D. Adams, who, because of their interest in chest



FIGURE 5 Postoperative Roentgenogram after Transthoracic and Transdiaphragmatic Resection  
*Note the clips of the non-Petz sewing machine where the stomach has been transected and the end turned in. The anastomosis of the now intrathoracic stomach to the lower end of the esophagus and the dilatation of the esophagus during peristalsis are shown*

that all gastric ulcers, provided the patient is a reasonably good risk, should be submitted to operation. This seems a radical position to take, particularly in the light of some of our previous statements, and some of our previous experiences with these lesions, which have healed under nonoperative management, but I have personally come to this conclusion for the following reason. The results in the surgical treatment of gastric cancers are so de-

diaphragm, repair of this defect has occasionally been necessary. It presents no technical problems of great difficulty except to be certain that the aperture is adequately closed without producing obstruction.

### PEPTIC ULCER OF THE ESOPHAGUS

Dr Donald T Chamberlain<sup>1</sup> has reported from this clinic the occurrence of 7 peptic ulcers of the lower end of the esophagus. One of these was due to the occurrence of a peptic ulcer in aberrant gastric mucosa, the remainder were associated with and probably brought on by hiatus hernia.

These lesions are probably brought about by the congestion in the mucosa as the upper end of the stomach and lower end of the esophagus rub against the edge of the aperture in the diaphragm, together

or duodenum as shown by the roentgenogram, one must have in mind the possible presence of such a peptic ulcer in the esophagus.

Dr Everett D Kiefer, of the Gastroenterological Department of the clinic, has set up the criteria for the diagnosis of these lesions: there must be a high



FIGURE 2 Roentgenogram of a Sizable Hiatus Hernia above the Level of the Diaphragm.

*It is quite well distended and in the state of distention that produces symptoms.*

with the fact that in the trapped segment of stomach there occurs a high gastric acidity, thus providing favorable conditions — congestion associated with gastric contents having high acid values — for the production of a peptic ulcer. These are the conditions that, when brought about in experimental animals, make it possible to produce experimental peptic ulcer (Fig 3).

In patients presenting typical ulcer symptoms with high acidity, hunger pain and food relief, and in the absence of any visible defect in the stomach



FIGURE 3 Roentgenogram of a Small Hiatus Hernia Associated with a Peptic Ulcer.

*The ulcer is shown by the fleck at the point of the arrow. Note the relation of this ulcer to the diaphragm, which can be seen as a shadow. This patient was relieved of all symptoms by ulcer treatment.*

gastric acid value, typical ulcer symptoms must be relieved by food and alkali, the ulcer must be visualized by esophagoscopy, and the symptoms must disappear after nonoperative ulcer management. All these patients have been successfully managed without operation, and the subject is discussed merely as a reminder of the occurrence of this lesion in a patient with ulcer symptoms but with no ulcer demonstrable in the usual locations.

### CARCINOMA OF THE CARDIA AND LOWER ESOPHAGUS

One of the lesions that has now become surgically approachable is carcinoma of the cardiac end of the stomach, so often spreading over onto the lower end of the esophagus, or vice versa.

The surgical management of these lesions by means of the transthoracic approach has been so

well established that everyone should be on the lookout to diagnose carcinomas of the upper end of the stomach or lower end of the esophagus earlier than they have been diagnosed in the past. Carcinomas of the lower end of the esophagus and upper end of the stomach, on the basis of autopsy figures from large hospitals, represent 5 per cent of

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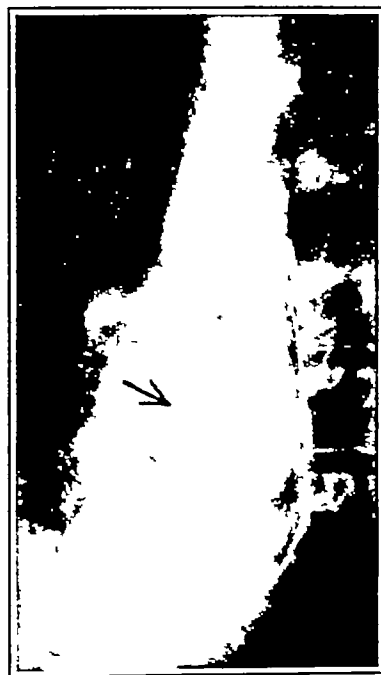


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pressing that there must be some radical change in our attempts to deal with them earlier if we hope to improve these results. It has now been demonstrated beyond reasonable doubt that even in the presence of gastric cancer, apparent healing of the ulcerating lesion can be brought about under good medical management. We have, in addition, in suspicious lesions found it difficult, and at times almost impossible, to make patients return a sufficient number of times for adequate check-up examinations to be certain that what appeared to be a benign lesion was not developing into a malignant

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As already stated, gastric carcinoma is almost the most depressing situation in the entire field of readily approachable surgical lesions. This is

TABLE 1 *Data on Resection of Cardia and Lower Esophagus*

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First (7/1/37 through 12/31/43)	28	16	9
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Totals	57	30	22



FIGURE 6 *Postoperative Roentgenogram after Transthoracic Resection*

*This illustration demonstrates how the duodenum has swung to the midline as the result of the altered position of the stomach and gradual traction on the duodenum.*

*Note again at the arrow the clips of the von Pez sewing machine, showing the transection of the stomach at its midportion.*

one. We have now done high subtotal gastrectomies on 85 consecutive patients with gastric ulcer with no mortality. In view of the above consideration, we believe that if this be balanced against the constant danger of wrongly diagnosing a gastric ulcer for early gastric cancer, better results will be obtained and greater progress will be made in the management of gastric cancer by the position of

primarily due to the fact that it is so rarely diagnosed early, which, in turn, is due to certain factors related to this lesion. It produces a low gastric acidity or an acidity and so does not produce the digestive symptoms related to high acidity, as occurs with ulcer; it is an infiltrating lesion and so does not produce early hematemesis, the stomach is of such size that the growth of the lesion produces obstructive symptoms only in the late stages of the disease. As a result of all these factors, the lesion may be fairly well advanced before it produces symptoms of an urgent and distinctive character.

In addition to the above factors, the high vascularity of the stomach, the rich field of lymphatics that surround it and the fact that it is a structure in which active and vigorous motion exists with great frequency produce conditions for early extension outside of the structure itself and result in recurrence today, in spite of radical operation, in over 90 per cent of cases.

To improve the results in carcinoma of the stomach will be difficult. It will involve requirements and conditions that are almost impossible to attain, that is, more complete and involved investigations for relatively minor symptoms, such as earlier gastric analyses, gastroscopies, fluoroscopies and roentgenograms, more frequent explorations of doubtful lesions and the more universal establishment of the position that I am now willing to take, namely, that all patients with gastric ulcer should be submitted to radical surgery.

The mortality figures for the last consecutive series of cases of peptic ulcer are submitted in Table 2, involving cases operated on in the last ten years.

#### GASTRIC CARCINOMA

Two types of operation are available for the management of gastric cancer—high subtotal gastrectomy and total gastrectomy combined with



splenectomy in order to make the total gastrectomy more radical and the anastomosis of the jejunum to the esophagus easier and safer under good direct vision, as can be done with the spleen removed.

Because palliative operations, such as palliative gastroenterostomy, are so unsatisfactory, are done so often in advanced lesions, provide relief for such a relatively short period of time and have such a high

involved nodes in the omentum, so frequently present in cases of carcinoma of the stomach, but also exposes the posterior wall of the stomach, the gastric artery at its root and the posterior wall of the duodenum so satisfactorily and adequately that it not only increases the radicalness of the procedure but makes it technically much easier to do.

### LEIOMYOMA OF STOMACH

In Figure 8 is shown the roentgenogram of a patient with leiomyoma of the stomach and in Figure 9 is shown the specimen of such a case, removed by subtotal gastrectomy.

I wish particularly to call attention to this lesion, of which we have now had 14 cases. I am especially anxious to call attention to this group of cases because almost all these patients have a history of repeated hemorrhages. In the removed specimen (Fig. 9) will be seen the healed scars representing ulceration of the mucosa over this tumor.

Because of the fact that leiomyomas usually do not produce symptoms except for the frequently profuse hemorrhages that go with them, this bleeding is often suspected of being caused by ulcer and, unless adequate investigation is carried out, many of these patients are treated for ulcer because of the profuseness of the hemorrhage.

It is important that these cases be diagnosed early because of the fact, as I have stated in a previous article on this subject, that 71 per cent of these tumors, on removal, have shown sarcomatous degeneration. It is for this reason that I particularly wish to call attention to them and their need for early and radical removal.

There has been no mortality in this group of cases.

### TOTAL GASTRECTOMY

Our oldest living patient on whom total gastrectomy was done was operated on October 8, 1937, for a large leiomyosarcoma involving all the stomach. She is, therefore, now alive and well eight years and seven months after operation. This operation, of which we have now done eighty-nine, is really a development of the last ten years. We have applied total gastrectomy in the cases of leiomyosarcoma in which it has the most favorable prospect of cure in that these lesions may involve the entire stomach but still remain of a relatively low grade of malignancy.

We have applied this operation also to the lymphosarcomas because of the fact that, with partial gastrectomy, it is difficult in many of these cases to determine the limit of infiltration because these lesions do not produce a true tumor, but are infiltrating in character. The oldest patient of this group is alive and well seven years and one month after total gastrectomy.

We have also applied this operation to the infiltrating type of carcinoma of the stomach to which

TABLE 2 Mortality for Cases of Peptic Ulcer (October 1, 1936, to April 1, 1946)

DIAGNOSIS	NO OF CASES	NO OF DEATHS	MORTALITY %
Duodenal ulcer	358	10	2.8
Gastric ulcer	65	0	0.0
Esophageal ulcer	67	2	2.9

mortality rate, we have been less and less interested in doing them. This has resulted in employing subtotal gastrectomy in many of the advanced cases of carcinoma of the stomach in which in the years gone by a palliative procedure, such as gastroenterostomy, would have been performed. This has been done on the basis that an operation in which the lesion itself is removed even when a cure cannot be anticipated is superior to a palliative gastroenterostomy in which the lesion is left behind, soon to invade the new stomach.

This approach results, as might be expected, in a relatively high mortality, 12 per cent in 256 consecutive cases, as may be seen from the statistics (Table 3). It is, however, superior to the palliative operation, in which the mortality is almost twice this figure, 21 per cent.

There are a few things that we have learned in our experience with subtotal gastrectomy for malignant tumors. One is that the operation can be made

TABLE 3 Mortality for Cases of Carcinoma of the Stomach (October 1, 1936, to April 1, 1946)

OPERATION	NO OF CASES	NO OF DEATHS	MORTALITY %
Subtotal gastrectomy	256	31	12.6
Exploration and biopsy	294	18	6.1
Palliative operation	66	14	21.1

more radical by combining omentumectomy with the subtotal gastrectomy, and the other is that to give these patients with malignancy a real chance, resection must be so high that it cannot be done with stomach clamps. For that reason, all subtotal gastrectomies performed at the clinic during the last eighteen years have been done with the von Petz sewing machine, making it possible to remove four fifths of the stomach in these cases, together with almost the entire omentum.

Omentumectomy, partial or complete, as shown in Figure 7, not only removes metastatically in-

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come sufficiently standardized in our hands and in the hands of many other surgeons so that it can be done with a reasonable mortality rate in spite of its magnitude, that patients can survive and live happily and maintain their weight and strength with no stomach and with the proximal loop of jejunum anastomosed to the esophagus serving as a substitute for a stomach and that it is necessary postoperatively throughout the remainder of their lives to keep close track of the blood picture in these patients, because of the tendency for anemias to occur. In almost all these cases it has been necessary for the patients to take liver, iron and vitamins. After operation, frequent meals must be

are as follows: 59.7 per cent have a chance of living for 12 months, 38.6 per cent for 18 months, 29.8 per cent for 24 months, and 21.1 per cent for 36 months or more.

### DUODENAL ULCER

Duodenal ulcer is the most complicated lesion in my opinion in the entire field of gastric surgery. In this clinic over the past years we have had passed through the Gastroenterological Department for management 8000 patients with duodenal ulcer, of whom approximately 6 per cent have come to surgery. The mortality rate was 1.5 per cent, but as a result of the occurrence of 4 fatalities in the last year is now 2.8 per cent for the past ten years.

This lesion, exclusive of gastrojejunal fistula, has associated with it the highest mortality rate in the entire surgical management of peptic ulcer. It will be noted in the statistical chart (Table 2) that in a consecutive series of 85 cases of resection for gastric ulcer there was no mortality, and that the mortality in 87 consecutive cases of resection for jejunal ulcer, which involves not only subtotal gastrectomy but also resection of the jejunum, was 2.3 per cent, even lower than that for subtotal gastrectomy for duodenal ulcer.

In discussing this lesion and its surgical management, I have again and again stated that the mortality of duodenal ulcer is not the result of the subtotal gastrectomy but of the relation of the duodenal ulcer to the head of the pancreas, into which it so frequently erodes, and to the common bile duct, to which it is so often intimately attached by the induration and scarring associated with it.

We have taken the position over the years that, when possible with reasonable safety, we should always remove the duodenal ulcer and that part of the duodenum in which it occurs. We do not believe that the removal of the duodenal ulcer is essential to bring about a cure with subtotal gastrectomy, but that its removal is often essential if one wishes to obtain enough flexible duodenal stump so that it can be safely inverted without the danger of a duodenal fistula. It has been our desire to avoid the occurrence of a duodenal fistula, representing as it does leakage, the danger of digestion of the fistula wall and the always possible occurrence of a fatality. It is for this reason, not the mere removal of the ulcer, that we have advocated that, included in the subtotal gastrectomy for duodenal ulcer, whenever reasonably possible, should be the removal of that portion of the duodenum in which the ulcer is situated, together with the ulcer.

Working, as we do, in very close and intimate relation to the members of the Gastroenterological Department of the clinic, it must be realized that practically all patients with duodenal ulcer coming to the Surgical Department for subtotal gastrectomy have ulcers of the chronic, recurring type, intractable to medical management and often asso-



FIGURE 8 Roentgenogram of a Leiomyoma of the Stomach. This shows the typical roentgenographic defect seen with these lesions.

eaten — at least five a day — until at least a year or more has passed, by which time, in most of the cases, three meals of sufficient size can be taken at the regular intervals that have been established for all of us, and the interval feedings will not be necessary (Figs 10 and 11).

Among the 89 cases of total gastrectomy there were 26 deaths, a mortality of 29.2 per cent, but of the patients operated on from January 1, 1942, through October 1, 1945, only 7 died, a mortality of 16.3 per cent\*. The estimated chances of survival, based on 57 patients who survived operation and were followed, whether now living or dead,

\*From follow up data compiled by Dr. Frances H. Smith, Department of Gastroenterology, Lahey Clinic (to be published).

the term "linitis plastica" has been given, owing to the fact that this type of cancer of the stomach, in contradistinction to the localized type, tends to spend its energy more largely in intramural infiltration than in local extension and metastases to the lymph nodes. The oldest patient of this group is now alive and well without recurrence five years and four months after operation.

As already stated, it is in the first group, the multiple leiomyosarcomas involving the entire stomach, that there is the greatest prospect of cure by total

Our position regarding the use of total gastrectomy, therefore, can be stated in the light of our experiences to date with 89 cases in which this operation has been done. Even in cases with complete involvement of the stomach by carcinoma of the linitis plastica type, life can be and has been prolonged from a few months to five years and four months. In the linitis plastica type of carcinoma of the stomach cures cannot be expected, but prolongation of life with comfortable living can be anticipated in many of the cases, if properly selected. In lei-

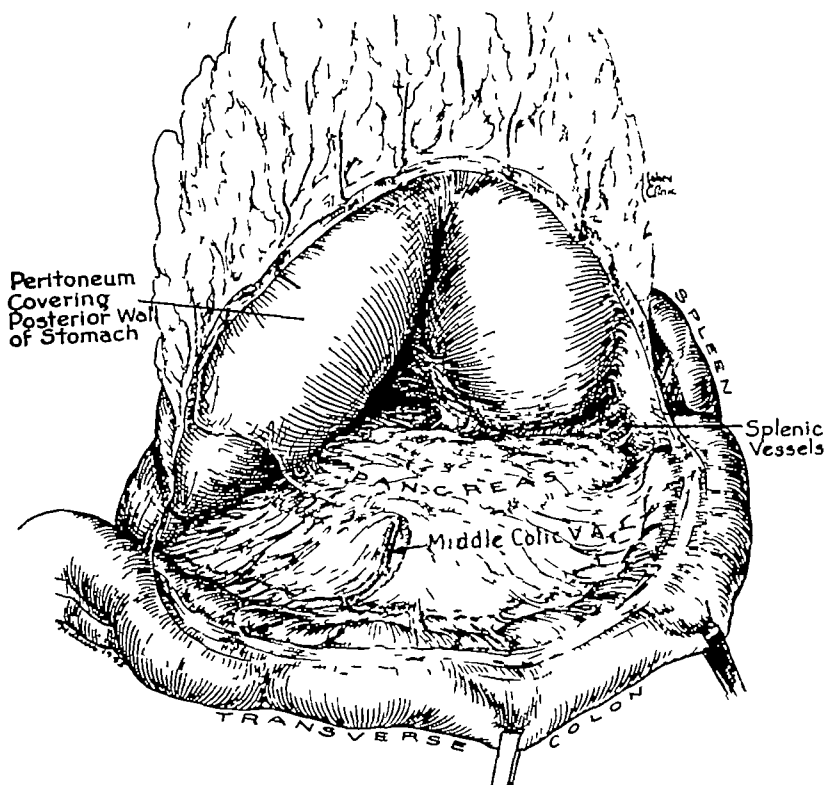


FIGURE 7

*This illustration shows how the omentum can be separated from the transverse colon for omentectomy, together with subtotal or total gastrectomy, and also demonstrates exposure of the posterior wall, the gastric artery and the posterior wall of the duodenum (reproduced from Marshall<sup>2</sup> by permission of the publisher)*

gastrectomy, and it is unlikely in the patients with carcinoma that there will be cases in which the lesions are so extensive that total gastrectomy is indicated in which permanent cures can be expected.

Although it is true that in the linitis plastica type of carcinoma of the stomach, obvious metastases to lymph nodes are often not apparent, it is in all probability equally true, in the cases in which the entire stomach is so involved that total gastrectomy is indicated, that there will be no cases in which some distant metastases have not already taken place and ultimate recurrence is inevitable.

myosarcomas there is a reasonable prospect of cure even when the lesions are extensive and total gastrectomies must be employed. Between the optimistic prospect concerning cure that one may have with patients who have leiomyosarcomas and the pessimistic ultimate prognosis in those in whom the linitis plastica type of carcinoma exists, rests lymphosarcoma of the stomach so far as the prospects of a satisfactory future life are concerned. This experience with total gastrectomy, as shown in our mortality figures, has permitted us to draw certain conclusions that the operation has now be-

come sufficiently standardized in our hands and in the hands of many other surgeons so that it can be done with a reasonable mortality rate in spite of its magnitude, that patients can survive and live happily and maintain their weight and strength with no stomach and with the proximal loop of jejunum anastomosed to the esophagus serving as a substitute for a stomach, and that it is necessary postoperatively throughout the remainder of their lives to keep close track of the blood picture in these patients, because of the tendency for anemias to occur. In almost all these cases it has been necessary for the patients to take liver, iron and vitamins. After operation, frequent meals must be

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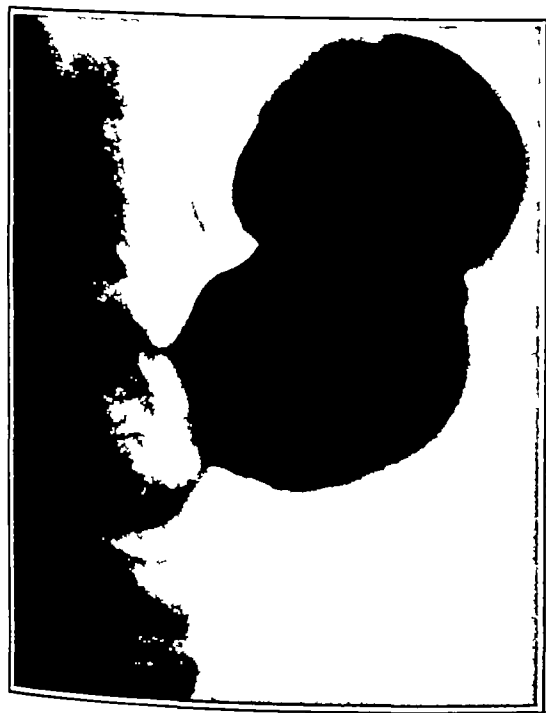


FIGURE 8 Roentgenogram of a Leiomyoma of the Stomach. This shows the typical roentgenographic defect seen with these lesions.

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ciated with complications, such as recurring hemorrhages or pyloric obstruction. This means that in a high percentage these patients on whom we do subtotal gastrectomy have badly scarred duodenal ulcers that have eroded into the head of the pancreas and into the pancreaticoduodenal artery, which runs on the back wall of the duodenum, and as a result of the induration and scarring, often have pyloric obstruction.

Over the years we have adhered quite strictly without much change to what we have published in

the hospital and in bed, where they have been relieved of emotional stress and strain, and by putting them on rigid dietary regimens and antispasmodics, with the result that in many cases the obstructions have been relieved, only to recur when the patients have resumed their work and activities under the stress and strain that frequently go with them, or when they have perhaps not adhered as rigidly to their dietary regimen as they should.

We have been disturbed at times by having to carry out surgical procedures on these patients late,

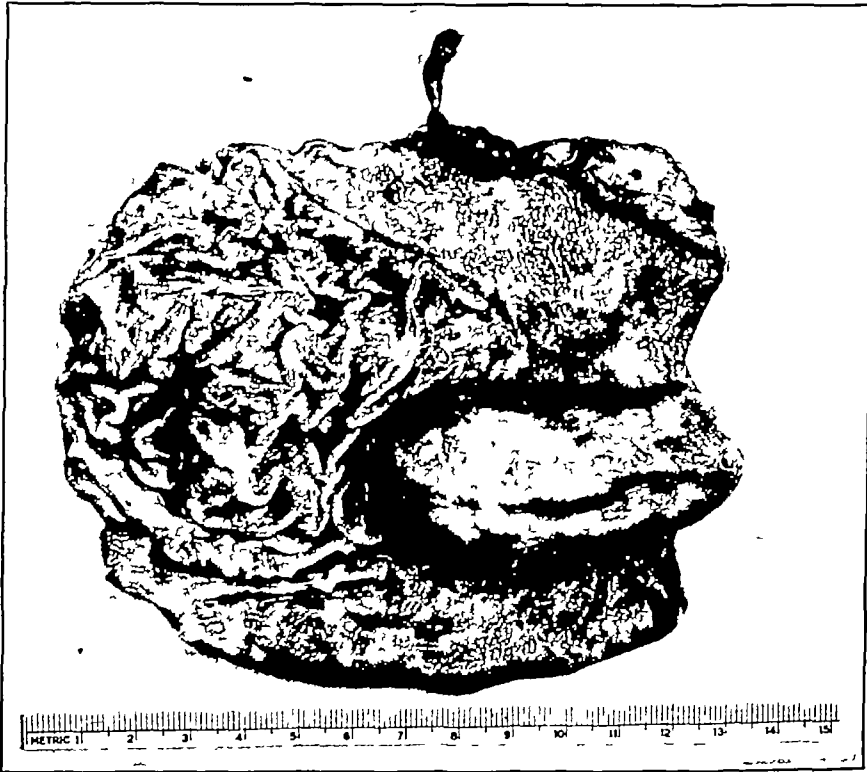


FIGURE 9 Gross Specimen of the Leiomyosarcoma

Note the scars of previous ulceration and hemorrhages, as mentioned in the text. Microscopically this proved to be a leiomyosarcoma.

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I have repeatedly said that in the past we have often wasted time and money of patients with recurring pyloric obstruction by getting them into

at which time we have often thought that we should have done the operations sooner. We have sought, therefore, a plan whereby we could make earlier decisions in the patients with pyloric obstruction, particularly those related to duodenal ulcer, concerning when we could expect that the pylorus that we are able to open would remain open, when it would not remain open and when surgery was indicated.

Dr S. Allen Wilkinson,<sup>4</sup> in the Gastroenterological Department, has developed and published a plan that has been of great help to us in making this decision. It consists of putting an indwelling Levine tube in the patient's stomach through the nose,

feeding the patient who is known to have pyloric obstruction a 90-cc noncurdling mixture through not decrease promptly within the three-day period from a high to a low figure, one can anticipate that

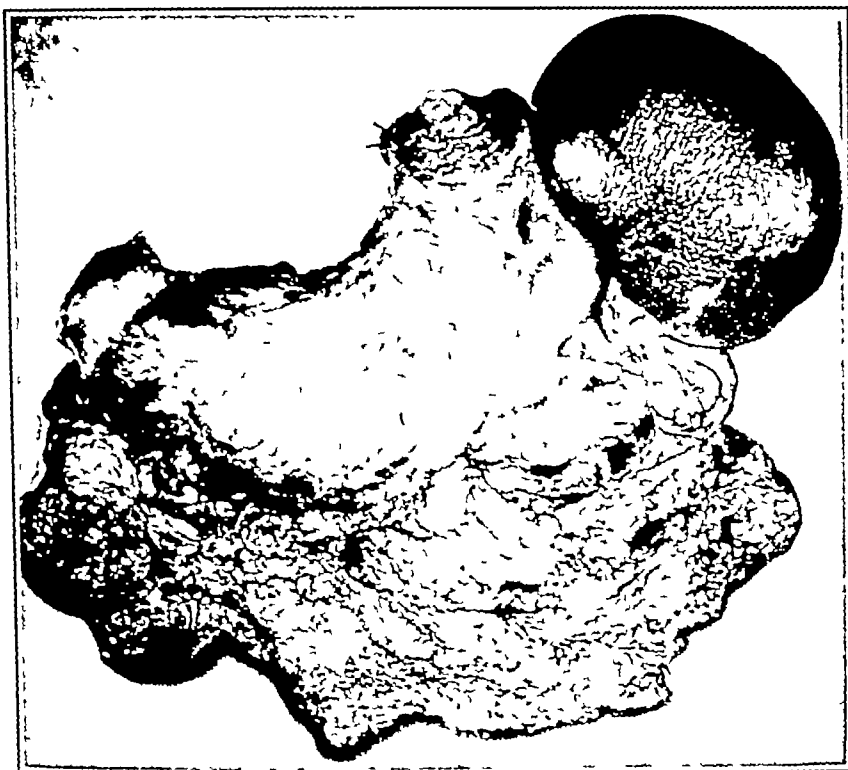


FIGURE 10 Surgical Specimen of a Total Gastrectomy for Carcinoma of the Linitis Plastica Type

Note the entire removal of the stomach, the small cuff of duodenum with all of the omentum attached and the spleen

the tube every hour for twenty-four hours and continuing this for three days. The tube is clamped for the first half-hour of each hour and is drained for the second half-hour, and the total amount of drainage obtained is recorded at the end of twenty-

the pylorus will not remain open and surgery will be necessary.

It is to be noted also in these patients who have pyloric obstruction that there is a time relation to the probability whether the pylorus will remain

TABLE 4 Results of Tube Drainage in Nonoperated Cases of Duodenal Obstruction

CASE NO	DURATION OF OBSTRUCTION	6-Hr RESIDUE %	TUBE DRAINAGE* cc/day	RECURRENCE
1	6 mo	90	41-24-18	1 yr (operation)
2	2 mo	Large	34-33-7-2	None
3	?	25	22-27-35-1-0	None
4	3 wk	90	50-42-24	1 yr (operation refused)
5	3 mo	Large	31-34-40	6 mo (operation)
6	?	Trac	33-19-18-10	None
7	10 days	Trac	25-22-30-9	Hemorrhage (2 mo) operation
8	4 mo	50	45-20-4	None
9	10 mo	Trace	26-22-6	None
10	2 wk	10	21-20-9-3	None
11	3 yr	50	44-41-50-41	5 mo (operation)
12	2 mo	70	24-1-1	None
13	2 yr	Not known	56-23-31-17-19	Operation refused
14	5 mo	90	20-3-1	6 mo (operation)
15	?	50	10-10-10-4	None

\*The figures represent the amounts on consecutive days

four hours. When, as shown in Table 4, which lists a few examples of such cases, the drainage does

open under medical management. Table 5 shows that in those patients who had pyloric obstruction

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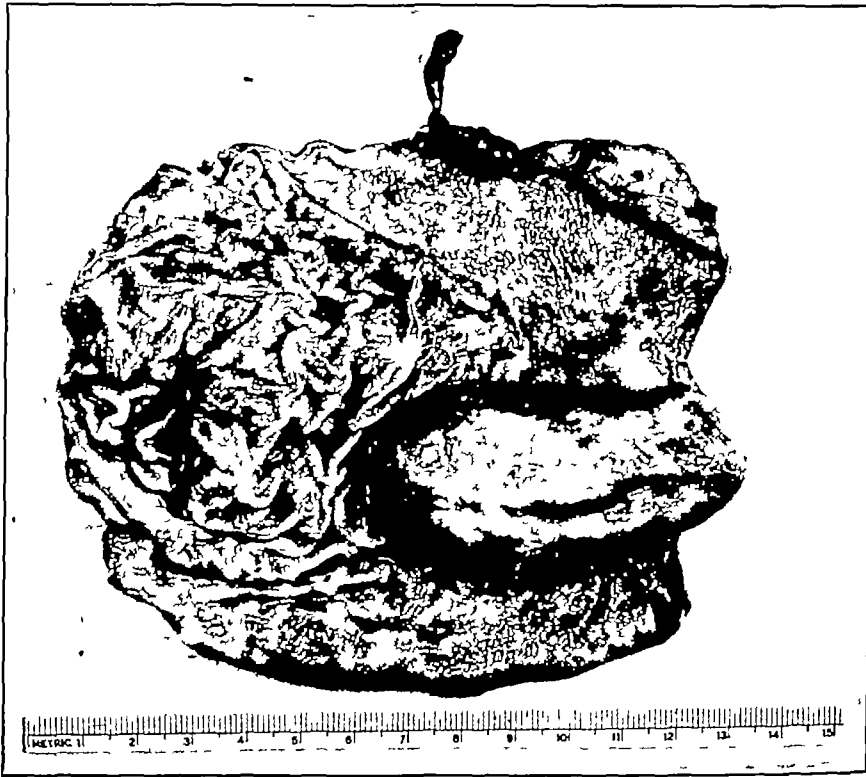


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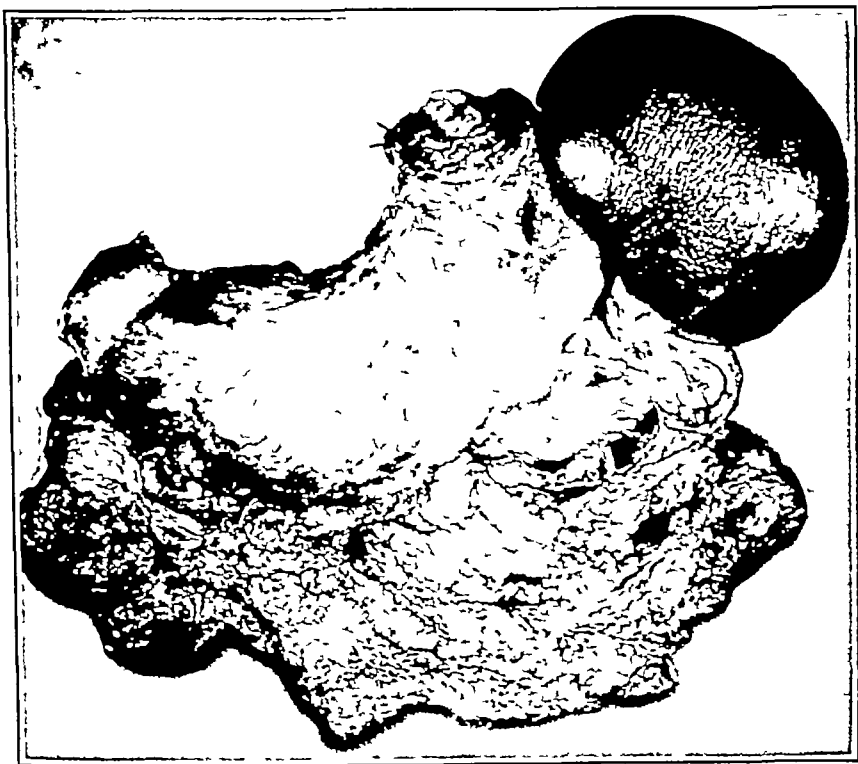


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open under medical management Table 5 shows that in those patients who had pyloric obstruction

for less than three months, 39 per cent<sup>4</sup> required ultimate surgery, whereas of those who had pyloric obstruction three months or more, an increased percentage (69 per cent) ultimately required operation. This has proved a valuable procedure in our hands in saving patients time in the hospital and permitting us to arrive at an early decision in patients with pyloric obstruction concerning when operation was necessary.

One should not leave the matter of bleeding without again calling attention to the fact that there are two types of bleeding associated with duodenal

concerning whether radical operation is advisable. It is our opinion, as stated above, that when such a hemorrhage occurs in spite of a good regimen of medical management, subtotal gastrectomy is indicated.

It is to be remembered, however, that there is another rare but extremely dangerous type of hemorrhage associated with duodenal ulcer — that

TABLE 5 Results of Drainage in 100 Cases of Duodenal Obstruction \*

DURATION OF OBSTRUCTION	OBSTRUCTION RELIEVED	OBSTRUCTION RECURRENT
	%	%
Less than 3 mo	61	39
More than 3 mo	31	69

\*Of these patients 56 were relieved by drainage and 44 were eventually operated on.



FIGURE 11 Roentgenogram Taken Several Months after a Total Gastrectomy

Note the dilatation of the jejunum to serve as a substitute for the stomach. Note also the two loops of jejunum with an enterostomy at the lowest point of the jejunal loop. There is no dilatation of the esophagus.

ulcer. The more frequent one, that with which everyone is quite familiar, is the case with an occasional single hemorrhage from which, in spite of a considerable loss of blood, the patient promptly recovers. Many patients with peptic ulcer become callused to hemorrhages of this type and do not look on them with undue apprehension.

In this type of bleeding there is no surgical emergency and the decision can be made deliberately

is, the massive hemorrhage in which the bleeding persists and is of such magnitude and frequency as to result not infrequently in a fatality unless something desperate is done.

It is in these cases that an immediate decision must be made if these patients are to be saved. This decision must be made within forty-eight hours and often within twenty-four hours if, in spite of massive transfusions, one hopes to save these patients. It is to be remembered that hemorrhage is often more serious and fatal in patients over fifty years of age than in those under fifty years of age. This is not an easy decision to make, but in the presence of persisting and repeated hemorrhages from duodenal ulcers, where facilities and adequate experience are available, these patients should not be permitted to go on to such desperate states that ultimate surgery, when done, has little or no prospect of resulting in anything but a fatality.

Decision regarding what the approach to this serious problem is must remain in the judgment of the surgeon, based largely on what the patient will stand. In some of these cases we have saved the patient's life by subtotal gastrectomy, together with removal of the indurated ulcer, and control of the bleeding, even when the risk has been desperate. In others, so desperate has been the situation that we have opened the duodenum, transfixed the bleeding ulcer with silk and done a gastroenterostomy to overcome the obstruction that has resulted. The mortality in these cases will be high. In this selected group with recurring massive hemorrhages it is the only procedure, however heroic the measure may appear to be, that offers these patients a prospect of life.

As a result of this experience with subtotal gastrectomies for intractable duodenal ulcer, we can draw the following conclusions. The resection must be high (Figs 12 and 13) in order to get out the largest number of acid-bearing glands. Our resections

have taken out as a minimum three fourths and in most cases four fifths of the stomach, and when it is reasonably possible, it is desirable to remove the ulcer and that portion of the duodenum in which it is situated. An antecolic anastomosis without enteroenterostomy has in our hands been the most satisfactory method of restoring the intestinal stream, it is not desirable to do an enteroenterostomy between the afferent and efferent loops of jejunum because of the fact that it sidetracks alkali-

It is well to state to these patients that following subtotal gastrectomy they cannot eat anything they desire and cannot drink and smoke. If they wish to have the best prospect of nonrecurrence of their ulcers, in the form of gastrojejunal ulcers, they must remain on a postoperative diet that is almost as rigid as is the diet for the medical management of an ulcer that is to be treated without surgery. It must, I believe, be accepted that if a patient has once had an ulcer he is a prospect for

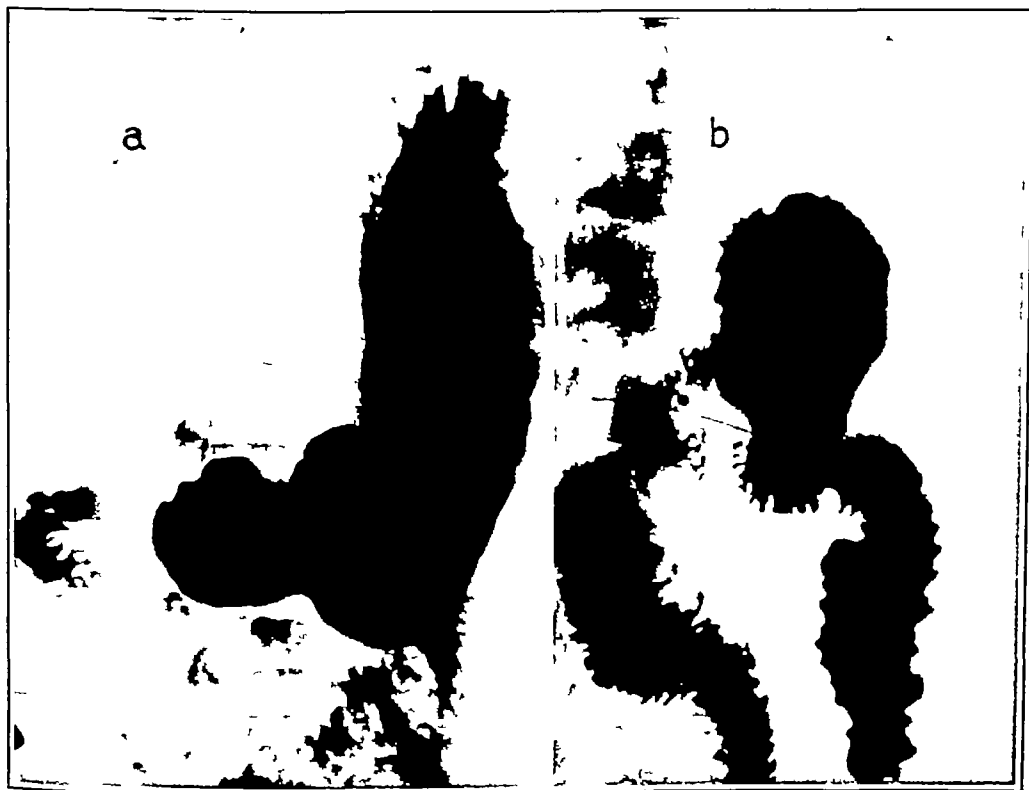


FIGURE 12 Roentgenograms in a Case of Duodenal Ulcer

*The one on the left was taken preoperatively. That on the right was taken after a high subtotal gastrectomy. Note the Hormeister type of anastomosis, the small traction of stomach remaining and the absence of any enteroenterostomy. These anastomoses are all of the antecolic variety.*

line duodenal and jejunal contents beyond the stomach and prevents them from entering the stomach, as they do when no enteroenterostomy is done, thus helping to lower gastric acidity. When, as a result of subtotal gastrectomy, an acidity or acid values of 10 or below can be produced, there will be few if any gastrojejunal ulcers, and the end results will be good. It is not necessary in our experience after subtotal gastrectomy to do jejunostomies or to introduce indwelling Levine tubes into the stomach, since these patients can be fed almost immediately after operation and, if adequate stomas are left, drain quite promptly and are not, in the majority of cases, bothered by postoperative vomiting.

another ulcer in spite of the high subtotal gastrectomy unless he takes every precaution in the way of change in his eating and living habits to prevent its recurrence.

#### JEJUNAL ULCER

Jejunal ulcer, sometimes called gastrojejunal ulcer, stoma ulcer or marginal ulcer, probably occurs in a much higher percentage of patients on whom gastroenterostomies for duodenal ulcer have been done than has been assumed to be true in the years gone by. What the exact incidence is, we cannot be absolutely sure, but it can safely be said to be over 15 per cent. In addition, as shown in our figures concerning the time gastrojejunal ulcer has

occurred after gastrectomy, it is not safe to assume that if a patient who has had a gastroenterostomy for duodenal ulcer goes three or four years, he is safe from the occurrence of this lesion. In patients coming here for surgery who have had gastro-

troenterostomy has been done that later closes, the closure is the result of the cicatrix that follows the spontaneous healing of a gastrojejunal ulcer. We have several times seen such scars about the marginal stoma that brought about closure and must have been due to a healing of a previously existing gastrojejunal ulcer.

We believe that there is but one indication for immediate surgery in gastrojejunal ulcer, and that is when, as shown in Figure 14, it can be demon-



FIGURE 13 Roentgenogram of a Patient Who Developed a Gastrojejunal Ulcer after a Subtotal Gastrectomy

The first operation, done elsewhere, was inadequate, and a second subtotal gastrectomy had to be done. Compare the extent of this resection with the resection in Figure 12 to demonstrate the radicalness of the procedure employed.

enterostomies for duodenal ulcers gastrojejunal ulcers have occurred as late as twenty-seven years after operation.

Jejunal ulcer is known to be an intractable type of ulcer, and used to be thought to be so intractable that surgery should be employed in every case. We have now dealt with a sufficient number of these cases so that we know that some of them can be handled medically and that, under such management, the ulcers will heal. In fact, it is our opinion that some jejunal ulcers occasionally heal spontaneously without accurate medical management. It is in all probability true that when a good gas-



FIGURE 14 Roentgenogram Showing a Jejunal Ulcer Adherent to the Transverse Colon

This ulcer was ready to produce a gastrojejuno-colic fistula but, as proved by operation, it had not perforated.

strated that the jejunal ulcer is adherent to the transverse colon and in the process of perforating into the colon to form a gastrojejuno-colic fistula.

In 87 consecutive patients who were operated on for gastrojejunal ulcer, the operation consisting of a high subtotal gastrectomy together with resection of that portion of the jejunum in which the stoma and the stomal ulcer existed, the mortality rate was but 23 per cent, demonstrating again that this lesion, although one of a complicated character, has even a lower mortality rate than that of duodenal

ulcer, again because of the fact that subtotal gastrectomy in duodenal ulcer, as already stated, is so often complicated by the fact that the ulcer is adherent to the head of the pancreas and to the common bile duct

### GASTROJEJUNOCOLIC FISTULA

Gastrojejunocolic fistula is by all means the most serious lesion with which one deals in gastric surgery. It is a perforation into the transverse colon of a jejunal ulcer that has become adherent to the transverse colon, producing a fistulous tract varying in size from one that will barely admit a straw to an aperture, as shown in Figure 15, the size of a ten-cent piece

When large gastrojejunocolic fistulas occur, they result in a most undesirable physiologic state. They produce a condition that is comparable with pel-



FIGURE 15 Specimen Removed at the Second-Stage Operation for Gastrojejunocolic Fistula

The operation consists of partial colectomy, partial removal of the jejunum and subtotal gastrectomy. The gastrojejunocolic fistula is indicated by the arrow. Note its size and the amount of food that can be lost through it into the transverse colon.

lagra and a weight loss that is often startling. This is due to the fact that the constant escape of feces into the stomach discourages the desire for food and the constant escape of gastric contents into the transverse colon results in a pellagra-like state because it does not permit a good fraction of the food ingested to pass through the small intestine, where it can be absorbed for proper nourishment.

We have been through the employment of all types of procedures in an endeavor to handle patients with gastrojejunocolic fistulas successfully, and it was not until I devised the plan of cutting off the ileum at the ileocecal valve, turning the distal end in, and anastomosing the proximal end to the descending colon beyond the gastroenterostomy and

the fistula, with later subtotal gastrectomy and removal of the involved colon and jejunum, that we began to manage these cases successfully (Fig 16).

I devised this plan of procedure with the idea that I could so advance that portion of the fecal stream in the small intestine beyond the gastroenterostomy that less of the colonic contents would pass back into the stomach, that it would establish the fecal stream beyond the gastroenterostomy so that at

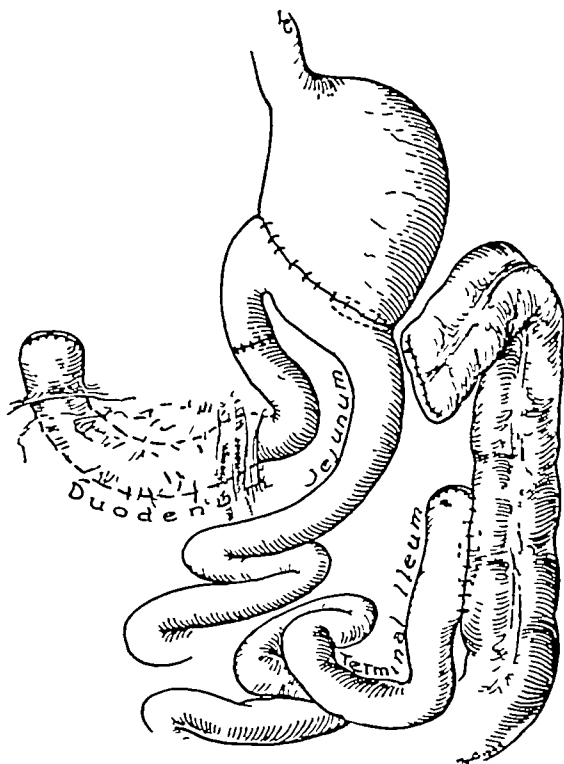


FIGURE 16

This illustration shows the completed procedure for handling subtotal gastrojejunocolic fistula. Note the anastomosis of the ileum to the descending colon, which is the first stage of the operation. At the end of three months these patients return, at which time the ascending colon, transverse colon and the section of the jejunum in which the ulcer and fistula exist are removed in one piece, and a subtotal gastrectomy is performed. This illustration shows the status of the gastrointestinal tract when both stages of the operation are completed (reproduced from Marshall's by permission of the publisher).

the second stage of the operation when the subtotal gastrectomy together with the removal of the involved colon was undertaken, the anastomosis between the descending colon and the terminal ileum would already have been established and functioning. This operation has been successfully applied in 20 cases. In 2 of these the anastomosis of the ileum to the descending colon, a procedure that diverts the fecal stream from the ascending and transverse colon, has resulted in spontaneous closure of the fistulous tract after the first stage of the

operation and has resulted in there being no necessity for doing the radical second stage of the procedure to remove the fistula and the jejunal ulcer, together with the transverse colon

It has been our experience in the remaining 18 cases in which the second stage of the operation has been done (Fig 16), that if these patients are sent home for two to three months following the anastomosis of the ileum to the descending colon, thus advancing the fecal stream beyond the fistula, they will return at the end of this time in much improved general condition, with a gain in weight and with such improvement that the radical procedure of the second stage can be employed with a reasonable prospect of survival

When one at first views this procedure, it appears to be so extensive as to unduly impress one with its magnitude. As we have done more and more of these operations, we have become aware that, with the fecal stream already established beyond the fistulous tract and with the patient in improved condition, it is possible, with reasonable ease, to cut the transverse colon off between the two rows of clips put in by the von Petz sewing machine beyond the fistula, just proximal to the splenic flexure, to turn the two ends in safety and to mobilize and devascularize the ascending colon and transverse colon, at which time the exposure becomes so adequate and complete that the operation, which consists of removing four fifths of the stomach, the involved segment of the jejunum and the ascending and transverse colon with the fistula into the splenic flexure, can be done more easily than the operation of subtotal gastrectomy and the removal of the jejunum alone in jejunal ulcer

This is an operative plan for this serious lesion that offers the following advantages: the prospect that in a small percentage of cases following the implantation of the ileum into the descending colon, the fistula will heal spontaneously and the second stage of the operation will be unnecessary, and the fact that the marginal ulcer, together with the fistulous tract into the colon and that portion of the stomach to be removed in the subtotal gastrectomy, can be removed in one block without spilling colonic contents and without the dangers of colon-bacillus contamination that go with any operative procedure

in which a fistula into the colon has to be opened and the fistulous tract into the colon closed

This procedure in our hands has made it possible to deal with these patients with gastrojejuncocolic fistula, who are so often emaciated and in extremely poor condition, more satisfactorily than with any other type of procedure that has been proposed

In the last ten years, this operation has been performed in 22 cases, with 2 deaths, a mortality of 9 per cent

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I have purposely avoided any detailed discussion of technical surgical procedures in this oration before this general audience

The mortality rates in the four types of peptic ulcer — gastric, duodenal, jejunal and gastrojejuncocolic fistulas — are given, as well as those of radical operations and of palliative operations for malignant lesions of the stomach

The type of lesions in which total gastrectomy has been applied in 89 cases and the total mortality in this group, together with the change between the mortality rate in the first 46 cases and that in the last 43 cases, are included

Some of the measures by which the now unsatisfactory end results of surgery for gastric cancer can be improved are stated

The mortality rate with transthoracic resection of the lower end of the esophagus and cardiac end of the stomach is reported again in two groups to indicate the improvement, as in total gastrectomy, that has come with added experience and improved selection

Hiatus hernia, peptic ulcer of the esophagus and leiomyoma of the stomach are discussed, as are gastric ulcer, duodenal ulcer, jejunal ulcer and gastrojejuncocolic fistula, and experiences and mortality rates in handling this group of cases are given

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## PRESIDENTIAL ADDRESS\*

### MOTIVATIONS AND OPPORTUNITIES

JAMES RAGLAN MILLER, MD †

HARTFORD, CONNECTICUT

**T**HERE are two kinds of motivation that incite men to activity — those that push and those that pull. Hunger, thirst, cold, want and fear are motivations of the “pusher” type. These are sufficient on occasion to furnish a certain amount of activity, even in the most indolent. The classic example of this type of motivation is the burr strategically placed near the rear end of the donkey. By reputation the burr is an effective measure in these circumstances to activate this obstinate animal.

On occasion the same obstinate donkey can be led along the path of progress by a “puller” type of motivation. A bit of hay located at the front end makes use of his weakness for appetizing fodder. This type of motivation is subtler than the first. It will not work if the animal is already fed or if the quality of fodder is poor, and it seems sometimes that the pure cussedness of the beast resists all stimulation, whether from the front or from the rear.

Physicians prefer to think that they are motivated by altruistic considerations of the puller type. Analogies like ripe fruit are good only for a brief period of ripeness, and although I should not have you think that I believe that medical organizations act like donkeys, I recall the elder statesman who in commenting on an approbrious epithet that one of his colleagues had used in reference to another said, “I should not classify our colleague by that term, but since it has been used I understand perfectly what is meant.” It will do us no harm occasionally to see ourselves as others see us, even though the exercise does not increase our self-complacency. The public has a high regard for the individual physician but is critical of us as a social group. To put it in the vernacular, they think that we have a “swell racket.” This criticism has, in a measure, crystallized in a series of socialistic provisions for medical care by government that you all recognize as centered in the Wagner-Murray-Dingell Bill. It appears to me that this threatening legislation, much as we dislike it, has nevertheless served as an effective pusher type of motivation, operating on organized medicine to produce not only resistance to the unsound legislation itself but to strengthen liberal movements within medicine that promise much for the good of society.

Meetings of the New England Surgical Society are usually devoted to the discussion of clinical

\*Read at the annual meeting of the New England Surgical Society, Boston, February 6, 1946.

†Visiting obstetrician and gynecologist, Hartford Hospital.

topics. Nevertheless, more than one president has seen fit to discuss some of the organizational problems that are encountered in the hospital, and it is my observation that the members have welcomed such a discussion. I too shall indulge in this exercise.

In his presidential address before this society in Hartford in 1932, Dr. Frank H. Lahey told us that if physicians do not take more interest in the management of the hospitals in which they work, they will gradually find themselves working not in but for those hospitals. This same advice holds good on the state and national level today. If physicians are to retain a dominant influence in the provision of medical care, they must raise their eyes more than occasionally from the sickbed or the operating table and help to solve the intricate problems of programming that are before us.

You are all familiar with the Hill-Burton Bill, which at present seems destined in some form to pass the present Congress. This bill calls for the study of the need for hospitals and health centers and provides for some construction where needed. It is important for us to remember that this bill as modified has the endorsement of the American Medical Association. When it goes into effect, we shall be compelled to think constructively in terms somewhat larger than has been our habit in the past, when our concern has been mostly with the management of our own individual hospitals. We shall have to plan for participation in a much more complex system of large and small hospitals, so integrated that skills and facilities can be made more generally available to the public.

In New England, as much as anywhere in the country, it has been a characteristic of the organization of medicine that it is decentralized and highly individualistic. I should be the last to wish to lose the advantages of this habit. We should, however, recognize some of its disadvantages and limitations. When physicians act as members of a group, they do so on three levels. The most significant group for the New England doctor is his hospital staff. Here the problems are almost exclusively clinical and have to do with the care of his patients. Next in order of significance in his mind is the local medical society or academy of medicine. He will attend its meetings if there is a good clinical program, otherwise not. Last of all comes his county or district association. This is the backbone of the guild organization, but here also clinical programs must be supplied to get a good attendance. Special regional

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ever, the financial condition of most of the states is extremely secure, and the state treasury is the natural source of help that should be developed in the future.

Now that the G. I. Bill of Rights is lifting part of the financial burden, I believe that it might be possible to obtain subsidies from state legislatures for a teaching program in hospitals possessing some of the features that I have outlined.

In Connecticut there has been much talk of establishing a medical department of the University of Connecticut. I do not know how far this movement will go, but it is stimulating to talk about it. If it were possible to buy a medical school and install it as one would an air-conditioning system in one's home, it might be that the cost would run to something between \$15,000,000 and \$40,000,000, including endowment. The cost, as you well know, would depend a good deal on the extent of the program and on the number of "ivory towers" that are built in. This, of course, would be the undergraduate medical school of the customary type, and I think that most legislatures would not be responsive to a program of such magnitude.

Although many persons, including myself, believe that an undergraduate medical school should be developed by the State of Connecticut, the need of the day, as I see it, is not so much for undergraduate medical education as it is for continued instruction after the doctor comes out of medical school. Postgraduate instruction should become a permanent part of the system of medical education, and its development should take place whether or not there is an accompanying undergraduate curriculum. Each should complement the other. No vast building program is necessary for such a program, for we already have the buildings, which are our own hospitals. All that is needed is a faculty, a large part of which is to be found in the hospital staffs. I am merely suggesting that these facilities be brought together in a more formal manner, placing on the governing board adequate representation of hospitals, medical societies, the university and the legislature. Medical teaching should be at three levels, those concerning the intern, the resident and the staff—which of course includes the courtesy staff. The university could furnish the dean's office and the academic

mechanisms for the program, and through it would come adequate compensation for those who carry on the burden of teaching. From the point of view of the intern and resident, the university could assure each one that he would get a training of high quality in his postgraduate years.

Tax-supported hospital systems have too often been veritable badlands of medicine. Exceptions to this rule are chiefly notable because they are exceptions. Now, badlands and deserts can be made to bloom by irrigation, and for the badlands of medicine the irrigation must be from the springs of medical education. This is the ray of hope that illuminates the future of the Veterans Administration under the plans of Generals Bradley and Hawley and our own General Cutler. Vast museums of living examples of various diseases in our state and municipal institutions are going to waste unused by our system of medical education. Is it not possible that this source of material can in some measure make up for the shrinkage of our ward services that has taken place under the influence of prepaid medical and hospital plans?

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In these few remarks I have made two suggestions that have admittedly been very incompletely developed. Each may stand alone, although together they are complementary.

First, organized groups of hospital staff officers might be developed into sections in the state medical societies. Second, postgraduate medical education is needed on three levels, those of the intern, the resident physician and the community physician. This could be developed at moderate expense by a combined effort of the medical societies, hospitals, a state university and the state legislature.

If imagination is needed to recognize the opportunity that lies before us, aggressive and courageous leadership will be necessary to develop it. Great generosity and largeness of spirit will be necessary to adjust many local and personal obstacles, but these are not times when medicine can afford to let the ambitions and prejudices of little men obstruct the proper development of all our resources to give full medical service to the public.

179 Allyn Street

and national societies also absorb the interest of many physicians, especially those who have the greatest capacity for leadership

Just at this point it appears to me there is an opportunity for us to develop a program, as in fact we must do under the Hill-Burton Bill, by enlisting the interest of many whose talents for organization have hitherto been developed only within their own hospitals. I believe that it should be possible in some way to bring together those who are concerned with matters of staff organization in hospitals and to make them realize their dependence on the welfare of the whole guild of medicine. Policies of staff relations to boards of directors, to community physicians, to insurance carriers and to plans for medical care and kindred topics would be eagerly discussed.

It should be possible for each state medical society at its annual meeting to arrange for a conference of hospital staff officers. In such gatherings discussion should be limited to matters of an organizational nature. I am familiar, of course, with the work that the American College of Surgeons has done along this line for many years. Dr. Walter G. Phippen and many another member of the Society have been interested, as you know, but so far none of us have been able to capitalize for the benefit of organized medicine the tremendous resources of ability that develop in hospital staffs. State medical societies could do their members a great service if they would recognize how deep is the interest of many of their members in these problems and how great would be the support for a section on hospital staff affairs if developed exactly as other specialties have been organized. Here also would be a forum for the discussion of the problem of the ordinary practicing physician who has no staff connections. Here too could be discussed many problems that arise in connection with prepaid medical and hospital plans.

Such conferences as I have suggested would hasten the day when responsible staff members would sit at regular intervals throughout the year with the board of trustees of the hospital. Whether or not they have a vote is immaterial. Some hospitals have already established such intimate relations, although there are too many the staff and trustees of which view each other with a certain amount of suspicion.

The motto of such staff representatives might well be a paraphrase of the lines of Richard Lovelace: "Stone walls do not a prison make, nor marble halls a hospital." I do not have to labor this thought before the New England Surgical Society, but it is one that should be mentioned again and again in the councils of hospital management. Frankness, honesty, initiative, originality, clear thinking and seriousness of purpose are not items that appear prominently on the balance sheets of any organization, but they are ingredients failing which no institution can long survive, and those who budget for hospital care must make due provision for their cultivation.

I believe that the time is ripe for us to make a bold experiment in medical education, one that may never have been contemplated in just the terms that I wish to propose. I am thinking particularly of our situation in the New England states, although some western states have developed certain of its features. Except in teaching hospitals and in a very few of the nonteaching centers, we must admit that the intern does not get a good postgraduate education. At least it is not nearly so good as we know how to give. He feels that he is merely an extra pair of hands with legs and fountain pen attached. Most of the nonteaching internships would not be selected by a physician for his own son except perhaps in his own hospital, with the hope of thus assuring him a speedier and easier entrance into local medical practice.

In the report of the subcommittee on intern curriculum prepared for the Connecticut Postwar Planning Board's Committee on Medical Care and Health, the following statement was made:

The studies initiated by the committee were for the purpose of determining how intern service in many Connecticut hospitals could be improved and made more attractive, to the end that the recruitment of house staffs for Connecticut hospitals might be more adequate in the future and thereby increase the usefulness of the hospitals and attract well trained physicians to the state for intern training, with the possibility that they might permanently locate in practice here to make up natural losses.

Among other things the committee recommended the employment of full-time or part-time medical personnel to cover the fields of pathology, radiology, anesthesiology and psychiatry for all hospitals of more than 100 beds. For those of more than 200 beds it was recommended also that a full-time physician be employed as a teacher to co-ordinate the hospital's educational program for interns, residents and staff members.

Such a program comes face to face with practical considerations of financing. Only a small part of it may be added to the patient's per diem charges, although he benefits from it directly as well as indirectly. If a satisfactory teaching program is developed, even though every expedient be employed to activate the voluntary services of the unsalaried staff, the costs will be more than can be borne without subsidy from private or public sources.

Medical schools that in the past have kept income and expense budgets on speaking terms with each other are greatly concerned with diminishing returns from private sources and are exploring the possibilities of government support. It is well known that the springs of private philanthropy are gradually drying up. Federal subsidies have not appealed to the New England mind because of the objectionable federal control that goes along with such subsidies, and if we are realists we should look at the huge national debt and become cautious when we think of federal subsidies in relation to long-range planning. In contrast to the federal treasury, how-

blood picture continued to improve, so that on February 15 it was believed that a transfusion would not be necessary, and only intravenous fluid was given. On that day the hematocrit fell from 32 to 29 per cent and the red-cell count from 3,240,000 to 2,350,000. For this reason blood transfusions were again started the following day, 500 cc being given daily for 3 successive days. For the next 2 days, February 19 and 20, the blood levels maintained themselves, but on February 21 the hematocrit fell from the 32 per cent of the previous day to 29 per cent, with a corresponding drop of the hemoglobin and red-cell count. There was no rise of the

The subsequent course was one of gradual improvement in both the clinical and laboratory findings. No further transfusions were required. The patient was given large doses of oral and parenteral vitamins, ferrous sulfate and a high-vitamin diet. The red cells gradually increased in number, and there was a concomitant decline in the titer of cold agglutinins in the serum. The pneumonic process resolved slowly, but by March 28 the lungs were entirely clear on both physical and roentgenographic examination. Despite the complete clearing of the lungs, the patient continued to have low-grade fever, with a temperature between 99 and 100°F.

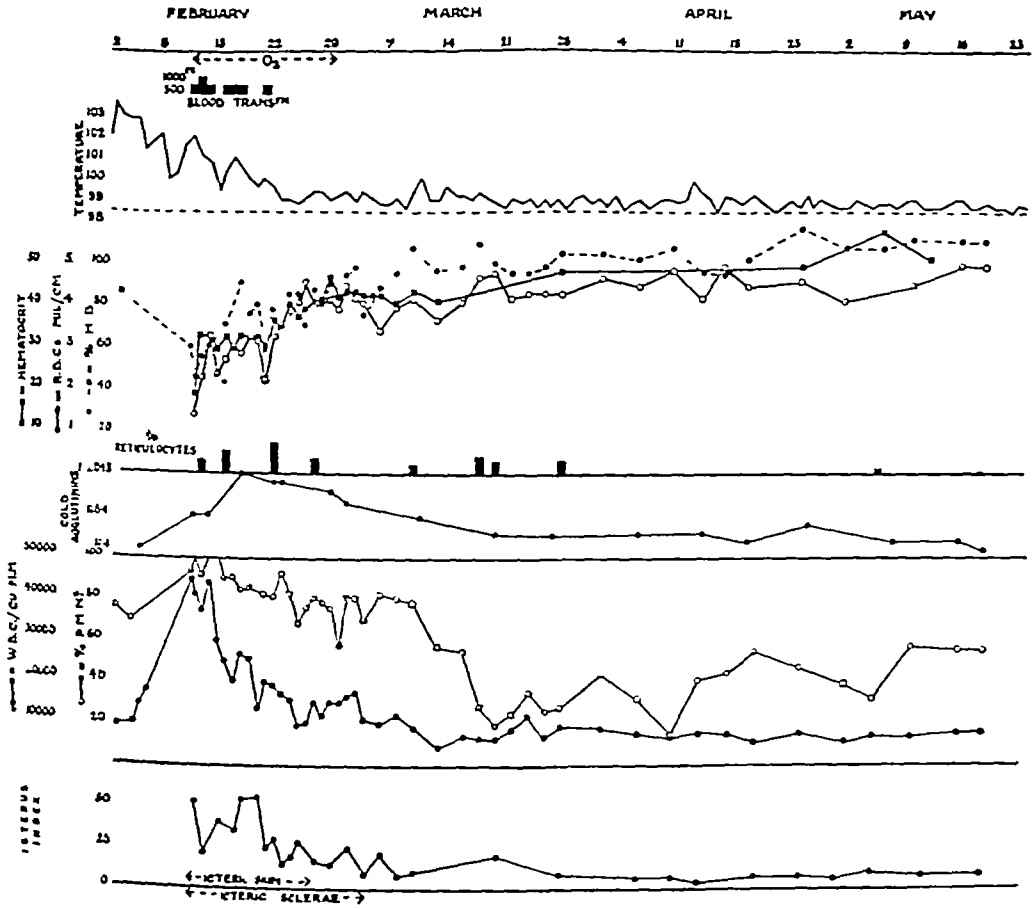


FIGURE 1 Clinical Course and Essential Laboratory Findings

stent index. Accompanying this fall in the levels of the red-cell components the patient stated that he felt weaker. He was sweating considerably, the pulse rose from 100 to 120, and dyspnea appeared prominent. The blood pressure was maintained. In the fear that another hemolytic crisis was imminent, 500 cc. of whole blood was again given, following which the pulse and respiratory rate diminished, and subsequently the patient was better. At that time the titer of cold agglutinins in the serum was 1:2048, this probably being the first correct titer obtained. On February 22 for the first time the lower border of the liver could be palpated as a rounded, nontender, firm edge 3.5 cm. below the right costal margin in the midclavicular line. The organ had been enlarged to percussion since February 17, and a definite sense of resistance in the right upper quadrant of the abdomen had been felt. The liver remained this size for 4 days and then began to recede gradually, so that on March 2 it could no longer be palpated. The spleen was not palpable throughout the course of the illness.

in the afternoon and evening. This continued on a diminishing level until he was essentially afebrile after April 21. At discharge on May 29, the patient was asymptomatic and the laboratory findings were normal. The cold agglutinin titer was 1:4. The patient was returned to full duty. This patient developed an acute hemolytic anemia with the presence of a high titer of cold agglutinins (autohemagglutinins), and the decrease of the anemia roughly followed a parallel course with the decrease of the cold agglutinins in the serum. None of the other factors that may cause such a hemolytic crisis were present. The Donath-Landsteiner phenomenon was absent, there was no acid-hemolysin, and no sickling tendency was present. There was a slightly increased fragility of the red cells to hypotonic saline solution.

# ACUTE HEMOLYTIC ANEMIA IN PRIMARY ATYPICAL PNEUMONIA ASSOCIATED WITH HIGH TITER OF COLD AGGLUTININS\*

## Report of a Case

MAJOR HAROLD S GINSBERG, M C, A U S

SEVERAL observers<sup>1-4</sup> have reported cases of acute anemia occurring in patients with primary atypical pneumonia who have developed high titers of cold agglutinins (autohemagglutinins). Since all these patients, with 2 possible exceptions, had been given one of the sulfonamide drugs, an additional etiologic factor was present that these authors thought might have been the primary or a contributory cause of the hemolytic crisis.<sup>†</sup> In the case reported below, no sulfonamide drug or any other medicinal agent was used that could have been an etiologic factor responsible for the causation of the acute hemolytic anemia.

### CASE REPORT

The patient, a 34-year-old soldier, was admitted to a United States Army general hospital on February 2, 1944 with a 24-hour history of increasing malaise, frontal headache, sore throat, cough slightly productive of yellow sputum, fever and chilliness, slight shortness of breath on moving about or talking and generalized muscle aches and pains. The past history was negative except for an episode of nasopharyngitis 3 weeks before the present admission.

On physical examination the patient was slightly uncomfortable and was coughing frequently. The cough was productive only of small amounts of frothy white-yellow sputum. There was slight tachypnea but no orthopnea and no dyspnea except with effort, and no cyanosis. The temperature was 102°F, the pulse 86, the respirations 19, and the blood pressure 122/82. The skin was extremely hot, dry and elastic, the color was good. Examination of the lungs revealed no abnormalities. The remainder of the physical examination was negative. The hemoglobin was 85 per cent (Tallqvist) and the white-cell count 9250, with 75 per cent neutrophils, 22 per cent of which were stab forms. Urinalysis and a blood Kahn test were negative.

The morning after admission the temperature was 103°F (Fig. 1), the respiratory distress on effort had increased somewhat, and the cough had become slightly more productive. Scattered, fine, moist, crepitant rales could be heard over the left upper lobe anteriorly. A portable roentgenogram of the chest revealed a patchy density of the left upper lobe and the upper portion of the left lower lobe. The sputum smear and culture revealed no pathogens, and blood culture showed no growth. There soon developed slight dullness over the entire left lung, and numerous rales were heard throughout it. The white-cell count began to climb slowly, but owing to the fact that the sputum never assumed the characteristics of a bacterial pneumonia by gross examination, direct smear or culture, sulfonamide therapy was not begun. The titer of cold agglutinins in the peripheral blood on February 5 was +++++ in a dilution of 1:4.

Beginning on February 7, the patient began to feel much better, and the temperature appeared to be beginning a slow decline. The dyspnea and cough remained as prominent symptoms, and examination of the lungs showed no change. On February 9, the temperature for the first time fell to normal throughout the morning, and the patient felt greatly

improved. By the following morning, however, a new chapter proved to be commencing. At that time the patient stated that he felt much weaker. Dyspnea still appeared rather prominent, and he was slightly cyanotic, but the pulmonary signs were unchanged. That afternoon slight icterus was first noted, otherwise physical examination revealed no change. The liver was not palpable, and the patient seemed to be in no distress. On the following morning the hemoglobin was 60 per cent (Tallqvist) and the white-cell count was 44,350, with 93 per cent neutrophils, 37 per cent of which were immature forms. The urine was reddish-brown, negative to the benzidine test and positive for bile and urobilinogen and gave a ++ test for albumin. The sediment showed 1 or 2 white cells per high-power field.

Within a few hours the hemoglobin was 45 per cent (Tallqvist), the red-cell count 1,360,000, the hematocrit 19 per cent, and the white-cell count 40,850, with 99 per cent neutrophils, 36 per cent of which were immature forms. Thus, the Wright-stain preparation of the blood smear revealed a typical leukemoid picture. Two nucleated red cells per 100 white cells were seen, and spherocytosis and polychromatophilia were noted. The red-cell count could be done only by first warming the diluting fluid. The direct platelet count was 451,520. The bleeding time was 6 minutes, and the clotting time 10 minutes, the clot retractility was good. The icteric index was 52. Urine urobilinogen was present in a titer of over 1:1000. There was bile in the urine but no blood. Bile was also present in the stools. Hemoglobinemia was present. Gross agglutination of the blood at room temperature was observed, even in high dilutions, this disappeared by warming above 37.5°C. Blood for determination of the titer of cold agglutinins was drawn, but could not be done for several days owing to lack of an adequate icebox. The Donath-Landsteiner phenomenon was negative. No sickling was observed in a sickle-cell preparation. No acid hemolysis was present in the serum. Blood allowed to clot and retract slowly at room temperature hemolyzed slightly.

Between the first laboratory tests and the completion of the second set of determinations the condition of the patient changed rapidly from that of a moderately uncomfortable patient to that of one who was so seriously ill as to be practically moribund. The blood pressure gradually fell from 124/70 to 100/44.

The typing of the patient's cells was not possible at incubator temperature, as well as at room temperature, owing to the high degree of adsorption of the agglutinin by the red cells, similarly, cross matching could not be performed. It was decided to use the specific type of blood, Type B, as determined by the patient's Army identification tags, rather than to use an uncross-matched blood of a universal donor.

Following alkalization the patient was given 500 cc of blood, which was kept warm throughout the transfusion. The blood was given over a period of 40 minutes, and no reaction occurred. Early the next morning 1000 cc of Type B blood was given, following which the patient appeared and felt much better. Blood taken for laboratory studies 1½ hours after the second transfusion revealed a marked improvement over the preceding day. An extremely slight increase in the fragility of the red cells to hypotonic saline solution was found. Agglutination of the blood at room temperature still occurred. The same afternoon the dyspnea seemed to be tiring the patient so much that oxygen by means of a mask was begun, from which the patient received considerable relief, both objectively and subjectively.

On February 14, rales were first heard over the right lower lobe and right middle lobe, they were fine, moist and crepitant and were scattered throughout these lobes. An x-ray film of the chest taken the following day showed coarse mottling throughout the right lung, the process on the left had cleared somewhat, but there were still fairly coarse, mottled densities in the upper third and lower half of this lung. The

\*From the Seventh General Hospital.

†Since this paper was prepared and submitted for approval by the office of the Surgeon General, Finland et al.,<sup>5</sup> in their series of papers on the laboratory and clinical features of cold isohemagglutinins, reported 11 cases of anemia of varying severity occurring in cases of primary atypical pneumonia having significant titers of cold agglutinins. In 4 of these, a marked drop of hemoglobin from 40 to 70 per cent occurring over a period of three days or less was noted, in 1 case no sulfonamide was given before the onset of the hemolytic anemia. Four of the patients in the entire group had received no sulfonamides before the development of the anemia.

## SUMMARY

A case of acute hemolytic anemia developing during the course of a severe primary atypical pneumonia that developed a high titer of cold agglutinins (autohemagglutinins) is presented. This patient received no sulfonamide therapy or treatment with any other drug that might have been the cause of the acute hemolytic process. Recovery occurred following repeated transfusions.

It is important to recognize that the pneumonias of the primary atypical type so prevalent for the last several years may develop a high titer of cold agglutinins that in themselves may be the cause of an acute hemolytic anemia as a serious complication.

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## MEDICAL PROGRESS

## HEMATOLOGY

WILLIAM DAMESHEK, M.D.\*

BOSTON

## THE SPLEEN

IN its normal state, the spleen is a relatively small organ weighing 50 to 100 gm and containing a variable amount of blood. Its function as a reservoir was thoroughly studied twenty-one years ago by Barcroft et al.<sup>1</sup> Removal of the normal spleen is followed by a number of interesting blood changes<sup>2</sup> — a tendency toward an increase in the red-cell count, the development of thin red cells (target cells) with increased hypotonic resistance, the development of Howell-Jolly bodies (nuclear remains) in the red cells and increases in the white-cell and platelet counts. These changes indicate a definite relation between the spleen and the blood-forming organs, notably the bone marrow, perhaps mediated by splenic hormones. The presence of red cells with nuclear fragments in the blood may indicate a splenic influence on denucleation of the red cell. Leukocytosis and thrombocytosis may be indicative of a spleen-granulocyte and a spleen-megakaryocyte relation. The development of thin red cells after splenectomy probably indicates that the mature red cells become thicker in their numerous but slow passages through the splenic sinusoids.

Although it is reasonable to assume that the spleen makes red cells thicker and thus prepares them for eventual breakdown so that they become more and more spherocytic, it is not known that the spleen actually destroys red cells. The old saying that the spleen is the graveyard of the red cells may require modification. Singer and Weisz,<sup>3</sup> by studying the bile excretion of normal and splenectomized dogs after phenylhydrazine hemolysis,

demonstrated that there was no decrease in the output of bile pigment in the splenectomized animals. Thus, in dogs at least, and under the conditions of these experiments, it seems that the spleen has little if any influence on blood destruction. These results, so contrary to the long accepted opinions on this subject, must be confirmed in other animals and by different experimental methods before they can become completely accepted. The life span of the erythrocyte, as determined in these experiments, was approximately one hundred and ten days, in line with the more recent investigations on this point. Thus, it appears that less than 1 per cent of the red cells are destroyed daily. The actual process of red-cell destruction in the normal animal is but little known and may be simply a matter of increased spherocytosis and gradual wearing down (fragmentation).

*The Spleen as an Endocrine Organ*

The spleen is not ordinarily included among the organs of internal secretion. Nevertheless, more and more evidence — to be sure, largely of the indirect type — is accumulating that the spleen produces hormones that enter the blood stream and have effects on remote organs, notably the bone marrow. The recent series of observations of White and Dougherty<sup>4</sup> indicate a hormonal relation between the adrenal cortex and lymphoid tissue. Ungar<sup>5</sup> recently isolated from the normal spleens of guinea pigs a crystalline substance that he called "splenin" and that had the property of causing a reduction in the bleeding time, an increase in the capillary resistance and an inhibition in the release of histamine from blood cells. It was found that the spleen participated in the endocrine response

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Owing to lack of facilities, it was impossible to perform several laboratory tests that might have been illuminating both during the acute illness and during the convalescence. The lack of them does not, however, detract from the important features in this case.

It was impossible to do the usual hepatic-function tests, so that the true status of the liver function during the acute illness, as well as during convalescence, could not be determined. There is, however, no clinical reason to believe that there was any decreased function at the time of discharge. The plasma proteins, prothrombin time and icteric index at discharge were normal, the hippuric acid excretion was slightly diminished (2.83 gm, oral test).

The cold agglutinins react as do other agglutinins in that they can be adsorbed by red cells at 0 to 5° C and in some cases even at room temperature, as was true in this case. The venous blood removed from February 12 and 14 was by an oversight allowed to separate slowly at room temperature, and without separation of the serum from the clot was placed in the icebox, which was at a temperature of about 10°C, until February 18, when the icebox was for the first time well enough regulated to maintain a temperature between 0 and 5°C, at which time these two serums as well as one drawn on February 18 were tested. The cold agglutinin titer of the later serum, which was separated immediately, the test being performed the same day, was 1:2048. Keeping in mind the fact that bloods drawn on February 12 and 14 showed autoagglutination at room temperature, we have every reason to believe that the actual titer in each serum was much higher than the test indicates.

Owing to the nonavailability of potassium dichromate at the time of the acute illness, it was impossible to make accurate standards for the determination of the icteric index. This accounts for the somewhat irregular curve of these determinations.

### DISCUSSION

The development of high titers of cold agglutinins (autohemagglutinins) was first reported in a large series of patients with primary atypical pneumonia of unknown etiology by Peterson, Ham and Finland.<sup>1</sup> This observation was confirmed by Horstmann and Tatlock<sup>2</sup> and shortly afterward by Turner, Nisnewitz, Jackson and Berney.<sup>3</sup>

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Antopol et al.<sup>5</sup> described 2 cases of acute hemolytic anemia with autoagglutination following sulfonamide therapy, one of which was a pneumonia of questionable type treated with Neoprontosil.

The mechanism of the acute hemolytic anemia in these cases of primary atypical pneumonia with high titers of cold agglutinins is still not clear, but the presence of this phenomenon without sulfonamide therapy helps to clarify it somewhat. It can be stated that the hemolysis in such cases as the one reported here is not due to a combination of a high titer of cold agglutinins and injury of the red cells by sulfonamides, as Dameshek<sup>3</sup> thought. Rather, the hemolysis may be due to agglutination of the red cells in the peripheral vessels, resulting in stasis, the hemolysis taking place as a result of trauma. Stats<sup>9</sup> has caused hemolysis *in vitro* by mild trauma while using blood and fresh plasma with a high titer of cold agglutinins. The agglutinins themselves may injure the red-cell membrane and thus make them more susceptible to the factors of stasis and trauma.

The fact that many cases of primary atypical pneumonia with extremely high titers of cold agglutinins do not have hemolytic crises still remains a complete mystery.

## SUMMARY

A case of acute hemolytic anemia developing during the course of a severe primary atypical pneumonia that developed a high titer of cold agglutinins (autohemagglutinins) is presented. This patient received no sulfonamide therapy or treatment with any other drug that might have been the cause of the acute hemolytic process. Recovery occurred following repeated transfusions.

It is important to recognize that the pneumonias of the primary atypical type so prevalent for the last several years may develop a high titer of cold agglutinins that in themselves may be the cause of an acute hemolytic anemia as a serious complication.

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quick return to normal or better than normal granulocyte levels. Splenic neutropenia may be completely idiopathic — that is, the cause of the splenomegaly may be quite obscure — or may be associated with the splenomegaly of certain cases of rheumatoid arthritis (Felty's syndrome), Boeck's sarcoid, Gaucher's disease, tuberculosis of the spleen, malaria and kala-azar. In any of these conditions, and in others with splenomegaly, the neutropenia may become so severe as to lead to recurrent bouts of infection and fever. Patients with this syndrome often go from clinic to clinic without a definite diagnosis, with their lives frequently in jeopardy on account of the frequent development of pyogenic infections. Splenectomy has been extremely effective in an increasing number of cases. Recent reports include those of Langston, White and Ashley,<sup>12</sup> Rogers and Hall<sup>13</sup> and Salzer, Ransohoff and Blatt.<sup>14</sup>

Splenic pancytopenia or panhematopenia — the latter is a term recently used by Doan and Wright<sup>15</sup> — includes cases of splenomegaly in which there is a simultaneous reduction in all the cellular elements of the blood. Many patients with splenic neutropenia have more or less marked thrombocytopenia or anemia or both. In these cases it is of great importance to recognize that the pancytopenia is not due to aplasia or hypoplasia of the marrow but is brought about by an inhibitory effect of the enlarged spleen on the bone marrow. Doan thinks that a phagocytic effect is responsible. Many of these cases go unrecognized for years because either the spleen is not felt or the pancytopenia suggests the presence of a hypocellular marrow. Sternal-marrow studies reveal hypercellularity of all the elements, with large numbers of nucleated red cells, granulocytes and megakaryocytes. If the diagnosis and interpretations of the marrow picture are correct, splenectomy is usually followed by a quick return of the blood picture to normal.

These views, although relatively new, are being rapidly bolstered by increasing numbers of clinical cases. Together with the other bits of evidence, chiefly drawn from pathologic material, they strongly indicate the presence of splenic hormones having at times deleterious effects on the maturation and delivery of cells from the bone marrow to the blood. There is need for more direct evidence bearing on these points.

#### *Rupture of the Spleen*

With enlargement of the spleen in certain infectious states, notably in malaria and infectious mononucleosis, spontaneous rupture may occur, causing the symptoms of hemorrhage, shock and an abdominal emergency. Russ and Gaynor<sup>16</sup> report the case of a soldier who had had a single attack of vivax malaria overseas. Eleven months later, in this country, he developed a malarial chill that was accompanied by acute pain in the left shoulder, which radiated to and was localized in the left upper

quadrant of the abdomen. Operation revealed a ruptured spleen and an abdomen filled with both fresh and old blood. Splenectomy was followed by recovery, but nine days postoperatively another chill occurred and *Plasmodium vivax* was recovered. Another case, also in a returned soldier, is reported by Kellner, Hochstein and Tillman.<sup>17</sup> In this case, shock quickly developed and the patient died before operation could be performed. At post-mortem examination, the abdomen contained 2500 cc of fresh blood. The spleen was extremely soft and presented a transverse laceration in its midportion, together with several other small stellate lacerations. It is advised that great caution be observed in palpating for the spleen in an acute attack of malaria.

Although infectious mononucleosis is almost always a benign disease and is subject to few complications, it is occasionally accompanied by serious symptoms. In a case seen with Dr. A. Grassi, of Haverhill, severe thrombocytopenic purpura developed, requiring splenectomy. Reports of splenic rupture are increasing in number. Davis, MacFee, Wright and Allyn<sup>18</sup> report a typical case of the disease in a young man who was suddenly seized with sharp pain in the left upper quadrant of the abdomen and in the left shoulder and developed the symptoms of shock. At operation, a wide longitudinal split of the splenic capsule was found, together with two tears in the pulp. The splenic disease was typical of infectious mononucleosis. Recovery ensued. Other cases have been described by King,<sup>19</sup> Darlev, Black, Smith and Good,<sup>20</sup> Ziegler<sup>21</sup> and Vaughan, Regan and Terplan.<sup>22</sup> Rupture in the last case took place with simple straining at stool. Martin<sup>23</sup> reports a case of ruptured aneurysm of the splenic artery.

Splenic rupture occurring spontaneously in an apparently normal spleen is reported by Duby.<sup>24</sup> A twenty-eight-year-old, married woman was suddenly seized with severe upper abdominal pain, difficult breathing and fainting. It was thought that she might have an ectopic pregnancy with rupture, and operation was therefore performed. Large amounts of intra-abdominal blood were found, and exploration revealed an enlarged, soft spleen with a large rent near the upper pole. Splenectomy was followed by recovery. The spleen weighed 340 gm and showed multiple lacerations. No cause for the rupture was obvious, and the splenic histology was unrevealing.

#### *Splenic Tumors and Cysts and Accessory Spleens*

Bostwick<sup>25</sup> reviews the 157 cases of primary neoplasms of the spleen in the literature and adds 7 of his own. Seven types are discriminated: angioma — either hemangioma or lymphangioma, lymphoma, reticuloendothelial neoplasm, embryonic inclusions, including various types of cysts, fibrosarcoma, leiomyosarcoma, and neurosarcoma.

A report from Argentina by Unchalo, Mainetti and Cuculicchio<sup>26</sup> concerns an interesting case of a

to tissue injury and played a part in the control of protein metabolism. These results, although they require amplification and confirmation, are among the first clear-cut and direct bits of evidence indicating the presence of splenic hormones.

The relation of "splenin" to "thrombocytopen," described a number of years ago by Troland and Lee,<sup>6</sup> remains to be determined. It appears both from clinical studies and from the study of extracts of spleens removed from patients with idiopathic thrombocytopenic purpura that the spleen in this disease contains a material, possibly hormonal, that has distant effects on the production of platelets from the megakaryocytes of the bone marrow. Since the platelet count becomes and remains extremely high following splenectomy in the normal animal and human being, and since splenectomy in idiopathic thrombocytopenic purpura is followed by a dramatic increase in platelets, it seems reasonable to conclude that the spleen in this disease contains an excess of the normal platelet-regulating substance. Idiopathic thrombocytopenic purpura may therefore be a form of hypersplenism. The frequent presence of thrombocytopenia in patients with splenomegaly and the return of the platelet count to normal or above normal following splenectomy afford clinical confirmation of this concept. The results with the injection of splenic extracts from patients with idiopathic thrombocytopenic purpura have been inconstant, about half the investigators confirming Troland and Lee's original observations and half reporting no reduction in platelets. Recent experiments in our laboratory with dogs as the test animals indicate the presence of an active megakaryocyte-platelet inhibitor in splenic extracts from patients with the disease.<sup>7</sup>

**Hypersplenism.** The spleen normally exerts definite effects on the bone marrow, causing both quantitative and qualitative changes in the blood cells. These normal effects, however, seem to have little significance, since the splenectomized patient can live a healthy, normal life with no shortening of the life span. But under pathologic conditions the spleen may develop unusual importance and may even be detrimental to life. When the splenic physiology becomes abnormal, various effects that are concerned with the bone marrow and blood may ensue. The bone marrow produces three types of cells — red cells, granulocytes and platelets. The splenic or hypersplenic effects, so far as they can be determined, are anemia, neutropenia, thrombocytopenia and various combinations of these conditions. Hypersplenism may thus be selective or total. If total, pancytopenia is present.

Splenic thrombocytopenia is the best known of the forms of hypersplenism. In many cases idiopathic thrombocytopenic purpura occurs suddenly, but in others it is prolonged, with remissions and relapses. Recent studies of the bone marrow by Dameshek and Miller<sup>8</sup> show that platelet formation by

the megakaryocytes is greatly reduced, but that following splenectomy it is greatly increased, leading to a rapid increase in the platelets in the blood. It appears that there is present in the spleen of patients with this disease an active material that causes inhibition of growth and delivery of platelets from the bone-marrow megakaryocytes to the blood. Thrombocytopenia may be primary or idiopathic, or it may be symptomatic of many conditions causing splenomegaly. Thus, in portal hypertension, — as in cirrhosis of the liver, — in disorders of fat metabolism (Gaucher's disease) and in chronic infectious splenomegaly the platelet count often becomes reduced, at times greatly so.

Splenic anemia has been discussed for years but has been largely discarded in the modern literature, chiefly because it became a blanket term covering many different disorders in which two features were present — anemia and splenomegaly. Many cases of leukemia, Cooley's anemia, sickle-cell anemia and so forth were called splenic anemia, until finally one investigator after another separated from this heterogeneous group different specific disorders. This left few conditions that could actually be designated as splenic anemia.

Abrami, De Gaudart d'Allaines and Dugas,<sup>9</sup> in a recent number of the French hematologic journal *Le Sang*, advocated revival of the term "splenic anemia" to include cases with splenomegaly and anemia in which splenectomy was therapeutically successful, apparently through the removal of an inhibitory effect of the enlarged spleen. Many cases of hemolytic anemia are cured by splenectomy. In some of these the red cells are defective, in a few, usually those in which the white-cell and platelet counts are also reduced, the spleen seems to be at the central point of the disease picture and splenectomy is dramatically successful. These cases are probably examples of hypersplenism with splenic anemia. Whether the spleen exerts only a hemolytic effect in these cases or also has an effect on maturation of red cells or their delivery from the bone marrow to the blood is not yet completely clear.

Splenic neutropenia is gradually becoming better known as a definite syndrome. This condition seems to be a form of hypersplenism in which the bone-marrow granulocytes are chiefly affected. First described by Frank<sup>10</sup> in 1916 under the term "aleukia splenica," the syndrome was revived more recently by Wiseman and Doan<sup>11</sup> under the designation "splenic neutropenia." Briefly, the combination of leukopenia, extreme granulocytopenia and splenomegaly is present. Pyogenic infections and fever are often present. Studies of the bone marrow rule out the presence of leukemia, lymphosarcoma and so forth and show increased numbers of granulocytes, despite the low granulocyte count in the blood. If the various studies and interpretations have been correct, splenectomy is followed by a

## THE HEMORRHAGIC DISEASES

As in previous reviews, the following classification of the hemorrhagic diseases will be used, chiefly because it seems both simple and physiologically accurate. It is based on the thesis that loss of blood from capillaries is ordinarily controlled by an intact blood-vessel lining, by abundant platelets and by certain plasma constituents, such as prothrombin, fibrinogen and thromboplastin. Hemorrhagic diseases may therefore be classified as follows: vascular purpura, in which there is a disturbance of the blood-vessel wall, thrombocytopenic purpura, in which there is a greatly diminished number of platelets, and disturbances of blood coagulation — hemophilia, hypoprothrombinemia, fibrinopenia and so forth — in which a defect is present in one of the several blood-clotting factors.

### *Vascular Purpura*

Bleeding into the skin in the form of ecchymoses and petechiae, unattended by a reduction of blood platelets, occurs under a variety of conditions — infectious or "toxic" — or for unknown cause. The large, purplish ecchymoses that have recently been so often observed in cases of meningococcemia are apparently due to the lodgment of meningococci in the skin capillaries and perhaps to some toxic influence on the blood-vessel walls. More frequent than these are the ecchymoses that many middle-aged women develop, particularly those with soft skins and rounded arms. These black-and-blue spots, often called "devil's pinches" because they occur spontaneously, usually appear in crops, chiefly on the thighs and arms. Their etiology is by no means obvious, although an endocrinal influence of some sort has been postulated. They have no particular significance and do not respond to vitamin, endocrine or other therapy. Of greater significance are the cases of vascular purpura in which crops of purplish ecchymoses occur about joints. These may be associated with renal disturbances. Histologic studies may disclose lesions resembling those of periarteritis nodosa. It is possible that such cases are related to such so-called "vascular" diseases as disseminated lupus erythematosus and periarteritis nodosa. There is evidence that the latter condition is a form of vascular allergy.

A blood-vessel disease that is familial and hereditary is hereditary hemorrhagic telangiectasia, first described by Osler, Rendu and Weber. Voyles and Ritchey<sup>34</sup> report 2 cases of this disease, which is characterized by the presence of multiple telangiectases, hemorrhage and anemia and a familial history. Their review of the literature disclosed 500 cases, occurring in about one hundred families. The hereditary factor is transmitted as a simple dominant and may affect either sex, atavism is occasionally noted. Epistaxes occur frequently, because the lesions that are often found in the nasal mucosa as well as in the skin and the mucous mem-

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may be of some therapeutic value when the blood prothrombin time becomes excessively increased with dicumarol therapy. Otherwise transfusions of fresh blood and large amounts of vitamin K are routinely used. Field and Link<sup>49</sup> found that the administration of large amounts of vitamin K protected rats against the action of dicumarol and in fact induced a temporary state of hyperprothrombinemia. Large amounts of 2-methyl-1, 4-naphthoquinone when administered to dogs, rabbits and rats were productive of hyperprothrombinemia lasting for several days. According to the observations of Spooner and Meyer,<sup>50</sup> dicumarol apparently not only affects the prothrombin time but also causes a reduction in platelet adhesiveness.

**Fibrinopenia** The rarest form of coagulation defect is that due to fibrinopenia or fibrinogenopenia. Henderson, Donaldson and Scarborough<sup>51</sup> report such a case. The principal features of this hemorrhagic disease are its hereditary character, a high evidence of consanguinity in the parents, its presence in both sexes, a total absence of fibrinogen in the blood and complete incoagulability of the blood. The disorder is probably caused by a hereditary defect in fibrinogen formation. Acquired cases, in which the disorder is due to a toxic or neoplastic interference with fibrinogen formation by the liver and bone marrow, may occur.

**Other disorders of coagulation** Pseudohemophilia is a hemorrhagic disorder that is occasionally encountered and that does not fit well into any one of the above groups. There is an increased tendency toward bleeding from minor wounds, the only constant defect found is a distinct increase in the bleeding time. The coagulation time may be slightly prolonged, and the recalcified clotting time may also be increased. The platelets are normal. Therapy by transfusions, splenectomy and so forth is without effect.

Evans and MacLaren<sup>52</sup> report the case history of a thirty-nine-year-old man who suffered bleeding from the skin, mucosa, and viscera. This disorder, they state, is a hereditary one affecting both males and females for at least four generations. No disturbances in coagulation time, bleeding time, prothrombin time or platelet count were present.

#### *Penicillin and Blood Coagulation*

Moldavsky, Hasselbrock, Cateno and Goodwin<sup>53</sup> studied the effect of penicillin on the coagulation, bleeding and prothrombin times in 20 patients. A marked reduction in coagulation time occurred in inverse ratio to the penicillin concentration. No change in prothrombin time took place. These authors suggest that penicillin is conducive to thrombus formation and may therefore be useful as a coagulant in certain hemorrhagic disorders. On the other hand, Hines and Kessler<sup>54</sup> found that penicillin sometimes caused a great increase in the effect of heparin in 2 cases of subacute bacterial endocarditis in which the latter drug was given as an adjuvant.

#### *Influence of the Contacting Surface on Coagulability of the Blood*

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salicylate The drug was discontinued and was resumed three weeks later Severe hemorrhages ensued in association with a low platelet level The megakaryocytes in the bone marrow were immature, with vacuolated cytoplasm and pyknotic nuclei Splenectomy was performed, but the patient died It is concluded that this was a case of allergic reaction to sodium salicylate with a direct toxic effect on the bone-marrow megakaryocytes In the absence of any evidence of hypersplenism, splenectomy could hardly be expected to have had an effect in such cases

Schwartz<sup>41</sup> describes the diagnostic and prognostic value of eosinophilia in the bone marrow in cases of thrombocytopenic purpura He believes that if the eosinophils exceed an arbitrary base line of 50 in relation to 1000 leukocytes of the metamyelocyte-polymorphonuclear series, the thrombocytopenia is of an allergic nature and will improve spontaneously without splenectomy With low eosinophil counts, however, spontaneous improvement is unlikely and splenectomy will probably be required Although these conclusions are based on the analysis of a fairly large series of cases, 30 in all, they require confirmation Nevertheless, the paper serves a highly useful purpose in directing attention to the possibility that certain cases of idiopathic thrombocytopenic purpura are allergic in nature According to our own experience,<sup>8</sup> the megakaryocytes in idiopathic thrombocytopenic purpura are increased but platelet formation is greatly diminished Following splenectomy, there is a remarkable increase in platelet formation by the megakaryocytes When there is active bleeding, the postponement of splenectomy may prove disastrous, because of bleeding into vital structures Carelli and Cangelosi<sup>42</sup> report a case of idiopathic thrombocytopenic purpura in which total blindness occurred, with active bleeding Splenectomy performed when the bleeding had become quiescent was productive of a rapid increase in platelets, but no improvement in the optic atrophy occurred This case points a valuable moral although there is some danger in splenectomy in acute thrombocytopenic purpura, it is usually better to accept it than to adopt a waiting policy

#### *Disturbances of Blood Coagulation*

**Hemophilia** It seems likely that methods for keeping in check the dread disease hemophilia will shortly be available The plasma-fractionation methods developed by Cohn and his collaborators at the Harvard Medical School have yielded an antihemophilic substance that has already been used experimentally by several groups of investigators At the Thorndike Memorial Laboratory, where much work on hemophilia has already been done, Minot et al<sup>43</sup> report on the effects of so-called "Fraction I" of plasma, which contains 60 per cent of fibrinogen, in 16 cases of hemophilia In 15 of these, the intravenous or intramuscular administration of

115 to 125 mg of the material was followed by a quick return of the coagulation time to normal Fibrinogen alone is without effect Intramuscular injections are at present associated with much pain Further work on this and other fractions is awaited with much interest, and it may well be that before long the hemophilic patient will be able to give himself daily injections of the deficient plasma fraction and thus maintain his coagulation time at normal values

Occasional cases resembling hemophilia occur in women One such case is reported by Madison and Quick<sup>44</sup> The patient had numerous serious hemorrhagic episodes All the features in this case except one — the recalcified coagulation time — were identical with those of hemophilia Quick had previously shown that the latter test is useful in differentiating a mild coagulation defect from true hemophilia In hemophilia, the rapid centrifugation of oxalated hemophilic blood, followed by recalcification of the plasma, is productive of slow coagulation, whereas with slow centrifugation rapid coagulation occurs In other hemorrhagic conditions, this difference does not occur

**Hypoprothrombinemia** The prolongation of the prothrombin time by the continued administration of salicylates was the subject of editorial comment in the *Journal of the American Medical Association*<sup>45</sup> Salicylates in large doses appear to act in a fashion similar to that of dicumarol and may thus cause a reduction in circulating prothrombin Severe cases of salicylate-induced hypoprothrombinemia may be associated with hemorrhage Large doses of vitamin K may either prevent the development of prothrombin deficiency or hasten its disappearance Pirk and Engelberg<sup>46</sup> found that quinine in ordinary dosage prolonged the prothrombin time, and suggested that the administration of vitamin K might be prophylactically beneficial in troops suffering bleeding wounds who were taking this drug An example of the rare condition of idiopathic hypoprothrombinemia is reported by Austin and Quastler<sup>47</sup> In this case severe and finally fatal hemorrhages took place All other causes of hypoprothrombinemia — deficiency of vitamin K, hepatic damage and dicumarol poisoning — had been ruled out

Hypothrombinemia continues to be utilized in some clinics as a prophylactic therapeutic method for the prevention of thrombosis following operation Dicumarol, the active principle causing sweet-clover disease in cattle, causes prolongation of both the prothrombin and coagulation times By careful observation of both these factors during administration of the drug, it is possible to maintain the coagulation times at high levels and thus minimize the dangers of thrombosis The dangers of hemorrhage have, however, not been fully controlled Jaques and Dunlop<sup>48</sup> noted that increases in the prothrombin time induced by dicumarol in rats could be shortened by adding calcium This

may be of some therapeutic value when the blood prothrombin time becomes excessively increased with dicumarol therapy. Otherwise transfusions of fresh blood and large amounts of vitamin K are routinely used. Field and Link<sup>49</sup> found that the administration of large amounts of vitamin K protected rats against the action of dicumarol and in fact induced a temporary state of hyperprothrombinemia. Large amounts of 2-methyl-1, 4-naphthoquinone when administered to dogs, rabbits and rats were productive of hyperprothrombinemia lasting for several days. According to the observations of Spooner and Meyer,<sup>50</sup> dicumarol apparently not only affects the prothrombin time but also causes a reduction in platelet adhesiveness.

**Fibrinopenia** The rarest form of coagulation defect is that due to fibrinopenia or fibrinogenopenia. Henderson, Donaldson and Scarborough<sup>51</sup> report such a case. The principal features of this hemorrhagic disease are its hereditary character, a high evidence of consanguinity in the parents, its presence in both sexes, a total absence of fibrinogen in the blood and complete incoagulability of the blood. The disorder is probably caused by a hereditary defect in fibrinogen formation. Acquired cases, in which the disorder is due to a toxic or neoplastic interference with fibrinogen formation by the liver and bone marrow, may occur.

**Other disorders of coagulation** Pseudothrombophilia is a hemorrhagic disorder that is occasionally encountered and that does not fit well into any one of the above groups. There is an increased tendency toward bleeding from minor wounds, the only constant defect found is a distinct increase in the bleeding time. The coagulation time may be slightly prolonged, and the recalcified clotting time may also be increased. The platelets are normal. Therapy by transfusions, splenectomy and so forth is without effect.

Evans and MacLaren<sup>52</sup> report the case history of a thirty-nine-year-old man who suffered bleeding from the skin, mucosa, and viscera. This disorder, they state, is a hereditary one affecting both males and females for at least four generations. No disturbances in coagulation time, bleeding time, prothrombin time or platelet count were present.

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An important complication in pernicious anemia is the development of polyposis and gastric carcinoma. Polyps seem to form rather readily in the atrophied gastric mucosa of patients with the disease, and malignant degeneration of the polyps is fairly frequent. From a statistical study of 293 post-mortem cases of pernicious anemia, Kaplan and Rigler<sup>61</sup> concluded that gastric carcinoma is three times as frequent in this group as in the general run of autopsied cases, the actual incidence being 12 per cent. It is suggested that frequent x-ray examination of the gastrointestinal tract be performed in cases of pernicious anemia.

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cyte is one hundred and twenty days — that is, that 0.83 per cent of the circulation is replaced daily. Harne, Lutz, Zimmerman and Davis<sup>64</sup> studied the life span of the red cells of monkeys by observing reticulocyte showers after hemorrhage and found it to be ninety-four to one hundred and seventeen days. Singer and Weisz<sup>65</sup> studied the same problem in the erythrocytes of dogs by observing the output of bile pigment in biliary fistulas of the renal type. By this method the average life span was found to be one hundred and ten days. In another article, Singer<sup>66</sup> reviews the various methods for determining the life span of the red cell and suggests that determination of this factor may be important in studying hemolytic anemia. By methods of cross determination — that is, by studying the survival time of normal red cells in the patient's circulation and that of his red cells in a normal circulation — it would be possible to demonstrate in a given hemolytic disorder whether the fundamental defect lay in the red cell itself or was extracellular.

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A case of hemolytic anemia in infancy, possibly congenital or possibly acquired, is reported by David and Minot<sup>78</sup>. During a hemolytic crisis the patient's serum showed the presence of an auto-hemolysin and an isohemolysin, which disappeared after splenectomy. The patient made a full recovery and behaved in most respects like most patients with acute hemolytic anemia of the acquired type. James and Evans<sup>79</sup> report a case of acquired hemolytic jaundice having its onset at the age of seventy and cured by splenectomy. Fourteen similar cases in patients aged fifty or over are discussed, five showed improvement after splenectomy. The risk of splenectomy in the elderly patient is naturally much higher than it is in the young one, acceptance of this risk is nevertheless essential if even one third of the patients are to be saved.

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In rare cases a dermoid cyst, usually of the ovary, is associated with severe hemolytic anemia

192 Beacon Street

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C CABOT

TRACY B MALLORY, M D, *Editor*

BENJAMIN CASTLEMAN, M D, *Associate Editor*

EDITH E PARRIS, *Assistant Editor*

### CASE 32251

#### PRESENTATION OF CASE

A fifty-two-year-old widow entered the hospital for study of a lesion in the left upper lobe of the lung.

Six years before admission a panhysterectomy had been performed on the patient at another hospital for carcinoma of the fundus of the uterus. Pathological examination revealed a pedunculated papillary adenocarcinoma of the fundus, with minimal invasion of the myometrium. After operation she was observed frequently until two months before admission, with negative results, at this time she had a cold, with a productive cough during which one sputum sample was blood streaked. A circumscribed area of increased density, 2 cm in diameter, had appeared in the base of the left upper lobe of the lung. Tubercle bacilli could not be demonstrated in the sputum. The cough disappeared shortly, but the lesion in the lung remained. There were no further hemoptyses, and she was asymptomatic at the time of admission.

Between the ages of forty-one and fifty the patient had frequently been observed at a sanatorium following the death of her husband from tuberculosis. At first there was a small area of productive infiltration in the first right interspace, which gradually cleared during the period of study. No lesion was ever seen in the left lung. There was also a long history of moderately severe hypertension, with one episode of dyspnea and ankle swelling. She had several anginal attacks over a period of many years. Four years before admission a right pyelotomy for renal calculi was performed.

On physical examination the vagina was deep, and there was a well suspended vaginal cuff. The cervix and uterus were not palpable. The vaults were clear, and rectal examination was negative. The cardiac rhythm was irregular, and a blowing systolic murmur was heard at the apex. The lungs were clear.

The temperature was 98.6°F, the pulse 80, and the respirations 16. The blood pressure was 190 systolic, 115 diastolic.

There were 14 gm of hemoglobin. The white-cell count was 8000. A rounded area of increased density 2 cm in diameter was visible in the chest film just opposite the anterior end of the fourth left rib in the basal portion of the upper lobe (Figs 1 and 2). X-ray examination of the skull, pelvis and long bones was negative. In the intravenous pyelogram 58 per cent of the dye was excreted in sixty minutes. The right renal pelvis as seen by retrograde examination was reduplicated. The lowermost group of calyces was less blunted than those in the upper group. The superior calyces were represented only by large, somewhat irregular cavities. A distinct defect consistent with an aberrant vessel was seen between the somewhat widened upper ureter and the pelvis. The calyces on the left were normal, but the pelvis was large. The ureter was normal. Ten red cells and rare white cells per high-power field were found in the right kidney urine sediment, and occasional red cells and three white cells per high-power field in the left.

An operation was performed on the thirty-first hospital day.

#### DIFFERENTIAL DIAGNOSIS

DR RICHARD SCHATZKI "An operation was performed on the thirty-first hospital day." The record does not say what kind of operation, whether it was on the kidney or the lung, but I suppose that it was performed on the lung.

Apparently I have been given the task of answering the time-honored question of the cause of a round shadow in the lung. Before we come to that, let us analyze the rest of the patient's history. We know that she had hypertension and angina. I do not believe that these need concern us at all. She had lesions of her kidneys. We had better look at the pyelograms. The intravenous and retrograde examinations were performed in a two-week interval. The films demonstrate what the record says—that both kidneys function and both look abnormal, the right more than the left. On the right side the kidney pelvis is bifid. The lower part of the bifid pelvis shows the dilatation frequently seen with an aberrant vessel. At the ureteropelvic junction one can see a defect that fits that diagnosis. The upper part of the bifid pelvis is not dilated, but there are large sacs representing markedly dilated calyces. On the left side, the calyces are fairly normal. The kidney pelvis itself shows some dilatation, which is not too remarkable. The appearance of the right kidney is consistent with what one sees in an aberrant vessel with extensive infection in the upper half of the bifid pelvis. We can say that this patient had pyelonephritis in the upper half of the kidney. Could this be tuberculous pyelonephritis? Since the patient was exposed to tuberculosis, I think that it could be, but a few facts make it a little unlikely. The first is that a number of years

before admission she had a pyelotomy and stones were removed from that kidney. Tuberculosis would probably have been diagnosed at that time. In addition, the kidney condition on admission was asymptomatic. That does not rule out tuberculosis, but tuberculosis is less likely than nonspecific pyelonephritis.

Another pathologic condition was a round mass in her lung. The two x-ray examinations were done six weeks apart, and the shadow did not change. On the lateral view the lesion seems clearly to lie in the lower portion of the left upper lobe. The

heart to the left. The hilar shadows do not look abnormal, and they are in normal position and of normal size. There is one helpful fact in the history: the patient apparently had a negative chest film two years prior to entry. At least that is what the record states. For the sake of discussion we shall assume that the interpretation was correct, which would automatically exclude a number of congenital lesions, or some slowly growing lesions. In other words, there was a round mass, which developed in two years. This lesion was first discovered when the patient had a so-called "upper



FIGURE 1 X-Ray Film of Chest  
*The arrow points to a rounded area of increased density*

shadow is not quite round in the only lateral view that we have here. In addition to this finding I see two more abnormalities, which are not described in the record and which indicate that there is a slight decrease in the size of the left lung somewhere. On the lateral view there are a few streaks in the region of the lingula of the left upper lobe, which are less distinct in the anteroposterior view. The right lung, which normally extends posteriorly to the region of the spinous process, extends almost to the left edge of the spine, indicating that the right lung is too large and the left lung too small. In addition there seems to be a slight shift of the

respiratory infection" and had some blood-streaked sputum. The slight decrease in the size of the lung could conceivably be the residue of atypical pneumonia, which she might have had at that time, and could be merely a red herring so far as the lung lesion is concerned. Could the patient have had an infarct two months previously, of which this was the residue? The round mass lies in the middle of the lobe and not against the pleural surface, which automatically excludes an infarct.

If one leaves out queer and unusual things, one is left with three possibilities: tuberculosis, metastatic cancer and primary cancer of the lung. This

patient had been exposed to tuberculosis. Tuberculosis can produce a round single lesion in the lung. More frequently in the primary phase, but also in the reinfection type of tuberculosis, single or multiple round lesions are seen. From a roentgenologic viewpoint this could be tuberculosis. The exposure was many years back, the patient had repeated examinations in between showing a negative chest film, and the location was rather unusual for primary

assume that this lesion was metastatic, we must forget what we said about the decrease in the size of the lung. I assume that had nothing to do with the present lesion, which could be a metastasis.

Could this woman have had a primary tumor of the lung, a bronchiogenic carcinoma? It would be just about the smallest I have seen, but that is because we probably have not heretofore operated on them at that stage of the game, whereas we now do,



FIGURE 2 X-Ray Film of Chest  
The arrow points to a rounded area of increased density.

or reinfective type of tuberculosis, but still this may have been tuberculosis.

The patient had a carcinoma of the uterus removed six years before entry. Could this lesion in the lung be a metastasis? Cancer of the uterus may metastasize to the lung, and metastases may appear in the lung at such a late date, even though the primary tumor has been removed. How about the small hematemeses that the patient had? Can metastases produce bleeding? Yes, they can. Dr. King and Dr. Castleman\* have published some cases of involvement of the bronchial tree by metastatic tumor causing hemorrhage. If we as-

suming to the marked development of chest surgery. In years past we should have enumerated the possibilities that we are talking about now and said, "Let us watch." This could be a very small primary carcinoma of the lung, more or less in the periphery.

I am ending up where I usually end up with a single round lesion in the lung. From purely roentgenologic evidence, it is often impossible to make a differential diagnosis. This picture could be explained by any of the three possibilities that I have mentioned. That is my answer as a roentgenologist. As a clinician, I should probably take a guess, and I shall say that it was a malignant tumor.

DR. EDWARD B. BENEDICT: Would you consider a metastasis from a kidney tumor?

\*King, D. S. and Castleman, B. "Bronchial involvement in metastatic pulmonary malignancy." *J. Thoracic Surg.* 4:305-315, 1943.

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basis, we are on safe grounds in assuming that it was a metastasis from the uterus, which had been resected seven years previously.

## CASE 32252

### PRESENTATION OF CASE

A thirty-two-year-old housewife entered the hospital for study of a mass in the right lung.

One and a half years before admission the patient entered another hospital because of headache and weight loss. An area of density 3.0 by 2.5 cm was visible by x-ray in the right lower lobe. It was smooth in outline and homogeneous in density. The lung fields were otherwise clear. There had been no cough or hemoptysis. Bronchoscopy was negative. The patient refused operation and was discharged. During the next year and a half she was constantly fatigued, but lost no more weight. The headaches became less frequent and severer. The attacks were often associated with dizziness and mild nausea. Mild exertional dyspnea appeared in the last six months. One month before admission a mild hacking, nonproductive cough developed. There was no fever or sweating at night.

With the birth of a son thirteen years prior to admission, the patient had had "milk legs," which kept her in bed nine weeks. Early in this period there was a sudden sharp, pleuritic pain anteriorly in the left chest. This lasted a day and caused difficulty in breathing.

A cousin with whom the patient had close contact died of tuberculosis eight years before admission. At the age of twenty-four the patient had a bilateral salpingectomy. The pathological report was acute bilateral salpingitis. The periods thereafter were regular until admission, lasting from one to six days. The first day of the period was usually accompanied by cramping pains.

On physical examination there was a decrease in breath and spoken voice sounds over an area 4 cm in diameter to the right of the spine over the right lower lobe. The heart was normal. There was a healed midline suprapubic scar, with an area of slight tenderness around it. The cervix was long and normal. The uterus was forward and attached to the abdominal wall, was larger than normal and felt round. A hard, firm, irregular mass was palpated along the right side of the fundus.

The temperature was 99°F, the pulse 72, and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

The red-cell count was 4,180,000 with 12.7 gm of hemoglobin. The white-cell count was 7700, with 57 per cent neutrophils. The urine was normal. A x-ray examination of the lung revealed a mass just below the right hilum, probably in the right lower lobe. It had not changed in appearance from the original film. A flat plate of the abdomen and an

intravenous pyelogram showed normal urinary tracts. There was an ill defined, irregular mass in the pelvis slightly more to the right than left measuring approximately 11 x 6 cm in diameter. It did not appear to exert any pressure on the urinary tract. A barium enema was negative.

An operation was performed on the twelfth hospital day.

### DIFFERENTIAL DIAGNOSIS

DR DONALD S. KING: As Dr. Schatzki said in the preceding case, we are constantly faced with the problem of what to do with cases that show in the x-ray film, a small rounded area of density in the lung field. Within the last three weeks we have seen such shadows in 3 cases, similar to the one that is presented to me today. I should like to put up the films on these 3 cases along with the film of the case that I am to discuss. The first film is the film of today's case. Unfortunately there is only a Buckle film, which does not give the same density as an ordinary film. The lateral film in this case is also shown. As one notes the 3 other cases are different from the case under discussion in that the lesions are in the peripheral areas of the lungs and are not near the hilum. The first of the outside patients had a negative x-ray film in 1939. An x-ray film taken in 1942 showed the rounded lesion. Fortunately I was away at the time that this film was taken and did not have to decide whether anything should be done about it. We have other films taken in 1944 and 1946, which show that the lesion had changed very little if at all. The second case was one in which the lesion was picked up by routine examination of all the employees of one of the large Boston department stores; there were no symptoms of pulmonary disease. In the third case there were definite pulmonary symptoms, and the decision to operate will probably not be difficult.

In the discussion of today's case we note first the story of pleuritic pain that lasted a day and caused difficulty in breathing. There seems little question that the symptoms were due to a pulmonary infarct. I do not believe that there is any association between this episode and the rounded shadow that appeared some years later.

As in the case discussed by Dr. Schatzki, this patient was also exposed to tuberculosis, and the diagnosis of tuberculosis must therefore be considered. There is a possibility that the bilateral salpingitis was also of a tuberculous nature, but I assume that a pathological report of acute salpingitis rules out tuberculosis. Am I right in this, Dr. Meigs?

DR JOE V. MEIGS: Yes.

DR KING: "There was a decrease in breath and spoken voice sounds over an area 4 cm in diameter to the right of the spine." This examiner certainly made a careful examination. I shall wager anything that he had seen the x-ray films before he made that report.

DR SCHATZKI I should consider metastases from any tumor. We have the old one, adenocarcinoma of the uterus. I do not see a primary tumor of the kidneys in the films.

DR JOE V MEIGS Is it not unusual for a patient with carcinoma of the endometrium, a papillary type, without much invasion of the myometrium, to have metastases six years later? Most patients who have that sort of cancer do not have recurrences and metastases.

DR DONALD S KING I hope it is not cancer because if it is we must do a great deal of operating. It may be cancer and I should not want to be the one to say it is not. The case that I have to discuss in a moment is something of the same problem, and I brought down slides on 3 other cases that are waiting for a decision on this type of shadow. These 2 cases this morning will help us in making our decision. I shall guess that the diagnosis in this case is tuberculosis.

DR F DENNETTE ADAMS What about bronchoscopy?

DR TRACY B MALLORY The lesion was so far out in the periphery that it was not helpful. I do not know whether Dr Benedict expressed an opinion about this beforehand.

DR BENEDICT We were of the opinion that it would not show anything.

DR NICHOLAS MARTIN What about the possibility of adenoma of the bronchus?

DR SCHATZKI I do not believe that we have had a single benign adenoma of the lung that has not produced fairly marked bronchial occlusion.

DR MARTIN I disagree — not absolutely, but I think it does occur.

DR RICHARD H SWEET Before we discuss it any further might we not ask this question: Is it not true that adenomas are related to the large bronchi?

DR MARTIN Yes.

DR SWEET We have had one benign adenoma that was not in a large bronchus.

DR MARTIN I still think we have to list it as a possibility.

DR SCHATZKI Would not the negative x-ray examination two years previously be against benign adenoma?

DR MARTIN Yes, that is a better reason.

DR SWEET Dr Schatzki and Dr King brought up what I consider an important point, namely, the utilization of surgery in some of these cases to make a diagnosis as well as to carry out treatment, because thoracic surgery is now on such a sound basis that we can operate in cases of this sort with a negligible risk. In recent years we have explored many of these patients whom, as Dr Schatzki said, we used to watch. Our preliminary diagnosis was tumor, probably metastatic. I was impressed, as Dr King and Dr Schatzki were, by the fact that if it was a primary carcinoma, it was certainly a very small one, smaller than any that I can recollect.

There was another factor that made the case interesting — the patient entered with the complaint of hypertension. Dr Smithwick was asked to see her about the possibility of treating the hypertension surgically. The question arose whether she might have the first stage of sympathectomy done at the same time as the lung operation. That was the question put to me. I did not see her until late in the course of the study. I was opposed to combining the two procedures because I believed that the tumor in the lung was of greater importance to this patient from the standpoint of length of life than the hypertension. I agreed that, if it turned out to be a simple procedure, we might do a thoracic exploration. We explored her and found an anomalous upper lobe. The peculiarities that Dr Schatzki mentioned are explained, I think, on an anatomical basis, because she had a lingula with an almost complete fissure. That fissure was subdivided to correspond to the two branches of the lingular bronchus. It was a peculiar looking lingula. At the base of the proximal portion of one of the lingular segments was a tumor, which was obviously neoplastic. We thought first of doing a lingulectomy, but it was so close to where I had to resect that I decided that the safer and more conservative procedure was to do a left upper lobectomy. Because it was a simple operation, I allowed Dr Scannell, after I had completed the lobectomy, to do a sympathectomy, which he did, and the patient made an excellent recovery.

#### CLINICAL DIAGNOSIS

Tumor of lung, probably metastatic

#### DR SCHATZKI'S DIAGNOSIS

Malignant tumor of lung

#### ANATOMICAL DIAGNOSIS

**Pulmonary metastasis from adenoacanthoma of uterus**

#### PATHOLOGICAL DISCUSSION

DR MALLORY The crux of the diagnosis rests on the histologic examination of this tumor. It was quite small, 2 cm in diameter, and very well circumscribed. A small bronchus ran into and terminated in the tumor, and the mucosa of this bronchus was slightly roughened by invasive tumor at the point of contact. On microscopical examination the tumor proved to be an adenocarcinoma, with a number of foci of squamous-cell metaplasia, the type of tumor ordinarily called an adenoacanthoma. This is a relatively frequent type of tumor in the uterus, much less usual in any other organ, and I cannot remember ever having seen it as a form of primary bronchiogenic carcinoma. We were eventually able to borrow a slide of the original uterine tumor and found that it also had the characteristic appearance of an adenoacanthoma. On that

basis, we are on safe grounds in assuming that it was a metastasis from the uterus, which had been resected seven years previously

## CASE 32252

### PRESENTATION OF CASE

A thirty-two-year-old housewife entered the hospital for study of a mass in the right lung

One and a half years before admission the patient entered another hospital because of headache and weight loss. An area of density 3.0 by 2.5 cm was visible by x-ray in the right lower lobe. It was smooth in outline and homogeneous in density. The lung fields were otherwise clear. There had been no cough or hemoptysis. Bronchoscopy was negative. The patient refused operation and was discharged. During the next year and a half she was constantly fatigued, but lost no more weight. The headaches became less frequent and severer. The attacks were often associated with dizziness and mild nausea. Mild exertional dyspnea appeared in the last six months. One month before admission a mild hacking, nonproductive cough developed. There was no fever or sweating at night.

With the birth of a son thirteen years prior to admission, the patient had had "milk legs," which kept her in bed nine weeks. Early in this period there was a sudden, sharp, pleuritic pain anteriorly in the left chest. This lasted a day and caused difficulty in breathing.

A cousin with whom the patient had close contact died of tuberculosis eight years before admission. At the age of twenty-four the patient had a bilateral salpingectomy. The pathological report was acute bilateral salpingitis. The periods thereafter were regular until admission, lasting from one to six days. The first day of the period was usually accompanied by cramping pains.

On physical examination there was a decrease in breath and spoken voice sounds over an area 4 cm in diameter to the right of the spine over the right lower lobe. The heart was normal. There was a healed midline suprapubic scar, with an area of slight tenderness around it. The cervix was long and normal. The uterus was forward and attached to the abdominal wall, was larger than normal and to the abdominal wall, was larger than normal and felt round. A hard, firm, irregular mass was palpated along the right side of the fundus.

The temperature was 99°F, the pulse 72, and the respirations 20. The blood pressure was 110 systolic, 70 diastolic.

The red-cell count was 4,180,000 with 12.7 gm of hemoglobin. The white-cell count was 7700, with 57 per cent neutrophils. The urine was normal. X-ray examination of the lung revealed a mass just below the right hilum, probably in the right lower lobe. It had not changed in appearance from the original film. A flat plate of the abdomen and an

intravenous pyelogram showed normal urinary tracts. There was an ill defined, irregular mass in the pelvis slightly more to the right than left measuring approximately 11 x 6 cm in diameter. It did not appear to exert any pressure on the urinary tract. A barium enema was negative.

An operation was performed on the twelfth hospital day.

### DIFFERENTIAL DIAGNOSIS

DR DONALD S. KING: As Dr. Schatzki said in the preceding case, we are constantly faced with the problem of what to do with cases that show, in the x-ray film, a small rounded area of density in the lung field. Within the last three weeks we have seen such shadows in 3 cases, similar to the one that is presented to me today. I should like to put up the films on these 3 cases along with the film of the case that I am to discuss. The first film is the film of today's case. Unfortunately there is only a Bucky film, which does not give the same density as an ordinary film. The lateral film in this case is also shown. As one notes, the 3 other cases are different from the case under discussion in that the lesions are in the peripheral areas of the lungs and are not near the hilum. The first of the outside patients had a negative x-ray film in 1939. An x-ray film taken in 1942 showed the rounded lesion. Fortunately I was away at the time that this film was taken and did not have to decide whether anything should be done about it. We have other films taken in 1944 and 1946, which show that the lesion had changed very little if at all. The second case was one in which the lesion was picked up by routine examination of all the employees of one of the large Boston department stores; there were no symptoms of pulmonary disease. In the third case there were definite pulmonary symptoms, and the decision to operate will probably not be difficult.

In the discussion of today's case we note first the story of pleuritic pain that lasted a day and caused difficulty in breathing. There seems little question that the symptoms were due to a pulmonary infarct. I do not believe that there is any association between this episode and the rounded shadow that appeared some years later.

As in the case discussed by Dr. Schatzki, this patient was also exposed to tuberculosis, and the diagnosis of tuberculosis must therefore be considered. There is a possibility that the bilateral salpingitis was also of a tuberculous nature, but I assume that a pathological report of acute salpingitis rules out tuberculosis. Am I right in this, Dr. Meigs?

DR JOE V. MEIGS: Yes.

DR KING: "There was a decrease in breath and spoken voice sounds over an area 4 cm in diameter to the right of the spine." This examiner certainly made a careful examination. I shall wager anything that he had seen the x-ray films before he made that report.

I assume, from the description of the pelvic examination, that there were two masses, one of which was the uterus itself and the other outside the uterus, but I cannot be absolutely sure of this from the description given

The most important sentence in the whole history of the case is in the x-ray report, which reads, "It had not changed in appearance from the original film" We are therefore dealing with an x-ray lesion that did not change in one and a half years The X-ray Department goes on to report, "An intravenous pyelogram showed normal urinary tracts" Obviously the doctors in charge of the case were looking for evidence of a hypernephroma from which there had been a solitary metastasis to the lung

I suppose again, as in Dr Schatzki's case, that the operation performed was an operation on the lung and not on the pelvis, and that we are again faced with the question of the nature of the round shadow My first inclination was to bet again on tuberculosis because of the story of exposure and because the symptoms were somewhat suggestive of a tuberculous infection But there are two things against this diagnosis In the first place, with a small rounded shadow that is due to tuberculosis, there is usually evidence of tuberculosis elsewhere in the lungs This is, however, not necessarily true In the second place, except in a calcified primary complex, the rounded shadows due to tuberculosis, or so-called "tuberculoma," usually change in appearance in eighteen months' time I believe that almost all the tuberculomas that we have observed have changed in the x-ray film in this length of time Am I right, Dr Sweet?

DR RICHARD H SWEET Yes, I agree

DR KING I am therefore inclined to say that the lesion under discussion is not tuberculosis

As I noted in the beginning, this rounded shadow is near the hilum of the lung where we have seen some bronchiogenic cysts, and some of the smaller cysts in this area have given somewhat similar x-ray appearance Usually, however, the area of density is larger and gives a somewhat different shadow I do not believe that this picture is sufficiently characteristic of a bronchiogenic cyst to warrant such a diagnosis

Primary carcinoma of the bronchus and metastatic cancer are both, I believe, ruled out by the fact that there was no change in the appearance of the x-ray film in a year and a half So far as our experience goes I do not believe that there has been a single case of primary or metastatic cancer of the lung in which the x-ray shadow has not changed in this length of time Even the hypernephromas, some of which are very slow growing, have changed definitely in that time

Of course I am concerned about the condition in the pelvis As I went over the case I was about to forget that there was anything wrong there, and until the discussion of Dr Schatzki's case I had not

given a thought to the possibility of a pulmonary metastasis from the pelvis Assuming that the operation was on the lung, it is quite obvious that the doctors in charge did not believe that there was pelvic cancer from which a metastasis might occur But I should like to have Dr Meigs discuss the possible diagnoses of the pelvic mass

DR TRACY B MALLORY You are wrong about that The operation was on the pelvis

DR KING This is, of course, a bombshell I was going to forget the pelvic disease so I am even more interested in what you think about the pelvis condition, Dr Meigs

DR MEIGS I have a note on the record that I shall try to find

DR FLETCHER H COLBY I am not convinced that metastatic lesions in the lungs necessarily change, as you say, in a brief period I do not know about one and half years

DR KING The only ones that I can be sure about are the ones that I have followed personally, and as I said, all of these have increased in size in a few months In the famous case of hypernephroma<sup>1, 2</sup> in which the kidney was first removed and the metastasis taken out several months later, with apparent cure after twelve years, the metastatic lesion had almost doubled in size in a year's time We have also recently followed a case in the Baker Memorial Hospital in which the hypernephroma was taken out five years ago and metastatic lesions appeared in the lung one year ago The lesions in the lung have unmistakably increased in size during the year's observation What the chest x-ray films might have shown if they had been taken in the four-year period before the metastatic lesions were discovered, I do not know

DR COLBY Some are fairly slow in growing They must be, because secondary deposits may appear even as late as fifteen years or more

DR KING I am going on the basis of my own experience in tumors like this

DR MEIGS I shall read part of my note "The cervix is long and normal in appearance The uterus is forward and attached to the abdominal wall, it is large and round — definitely larger than it should be The left side is negative, but in the right side I believe I feel a hard, firm, irregular mass This mass probably represents the right ovary, although with tumor in the lung I think we ought to consider that that might be a question of neoplasm Dr Benedict should be asked if he would like to peritoneoscope her If he does not, and all studies on your Service are negative, we would be very glad to explore her"

The question is, What kind of mass is it? Apparently she had no abnormal menstrual periods One would have to consider the possibility of a fibroid growing off the side of the uterus It might be in the form of leiomyosarcoma, which is a malignant tumor and may metastasize to the lung Pelvic



inflammatory disease we rule out because she had had both tubes removed. One would have to consider ovarian tumor, and it could even be endometrial cancer.

DR. KING: I should not have Dr. Meigs do my work for me, but I think it is fair under the circumstances.

We do not know what this lesion in the lung was then?

DR. MALLORY: Yes, we do.

DR. KING: And you know what the pelvis showed too?

DR. MALLORY: Yes.

DR. KING: I am now faced with the question of whether we can connect the two processes. I came determined not to consider the pelvis as a possible source of metastasis, and I shall keep to that line of approach. I do not believe that this is metastatic cancer, and I have already discarded tuberculosis and bronchiogenic cyst. The question that was raised about benign adenoma in the previous case interests me a great deal. Until 1942, except for one possible case, all the adenomas that we had followed were at least in part in the lumina of the larger bronchi and could be definitely proved by bronchoscopic biopsy. I had been told that while I was away there was a case admitted from another hospital in which operation had shown an adenoma that was entirely outside the bronchus. The case under discussion may be that case. I do not know. In view of the fact that this lesion has not changed in x-ray appearance in a year and a half and that it is close to the large bronchi, adenoma must be considered as a possible diagnosis.

There are a multitude of other benign tumors that should be mentioned, but it would be pure guesswork to try to name any other tumor. Fibroma, chondroma and hamartoma are all possible, but taking everything into consideration since I have to commit myself as to diagnosis I should say adenoma.

#### CLINICAL DIAGNOSIS

Adenoma of bronchus

#### DR. KING'S DIAGNOSIS

Benign adenoma of lung

#### ANATOMICAL DIAGNOSES

Adenoma of bronchus

Endometriosis of ovary

#### PATHOLOGICAL DISCUSSION

DR. MALLORY: The first operation was on the pelvis, and an ovarian mass was found to be due to

extensive endometriosis of the ovary. About ten days later the chest was explored, and Dr. Sweet will now tell about that.

DR. SWEET: This patient was admitted on the gynecological service, and I was asked to see her before the pelvic operation relative to what was wrong in the chest and whether anything should be done. I thought we had better see what was in the pelvis first because at that time we did give some thought to metastatic tumor. Having proved that the pelvic tumor was benign and therefore not responsible for the pulmonary lesion, we did go ahead with the chest operation. My reasoning was exactly the same as Dr. King's, and I came to the same conclusion on the same premise—that it was an adenoma. It was an interesting operation because when I first exposed the tumor it was in the lower lobe, presenting on the fissure as it lay against the middle lobe. I thought that I could excise the tumor locally. There was not much lung tissue over it. I believed that it was something I could pry out without difficulty, but in dissecting I saw that it was actually growing out of a bronchus and did a lobectomy. The further pathologic details we shall hear from Dr. Mallory, but I was convinced at the time that I was taking out an adenoma.

DR. KING: Was it inside or outside?

DR. SWEET: Both.

DR. MALLORY: I have the gross picture of the resected specimen. You can see the tumor without any difficulty, almost completely circumscribed, but as Dr. Sweet explained it was definitely adherent to the outer portion of the bronchial wall. There was no involvement of the bronchial mucosa and no narrowing of the bronchus by tumor. These tumors ordinarily arise within the bronchus, although they may also extend outward between the cartilages and form a dumbbell-shaped mass. This is a unique case, in our series at any rate, in that the tumor lay entirely outside the bronchus, with no projection in the bronchial lumen.

DR. MEIGS: This patient had bilateral salpingitis and endometritis eight years before admission. It is rare to see endometriosis under such conditions when the tubes are closed. This seems to refute Sampson's theory of menstrual blood flowing back through the tubes and producing endometriosis. If she had had the condition when she was first operated on it would probably have been noted.

DR. MALLORY: You might have noted it, but most surgeons do not see it as readily as you do.

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## TO THE MEMORY OF WALTER B. CANNON

ELSEWHERE in this issue of the *Journal* is a description of the Walter B. Cannon Memorial Hospital Fund. It is the purpose of this editorial to draw attention to this enterprise, and to point out how near the work to which this fund is to be devoted was to Dr. Cannon's heart.

For a number of years Spanish students worked intimately with Dr. Cannon in his laboratory, and when the lamentable overthrow of liberalism occurred in Spain, their continuing relation was greatly curtailed. Dr. Cannon had an instinctive, almost puritanical justice in his make-up, which overflowed with especial forcefulness when intellectual freedom suffered, particularly when the sufferers were imaginative young men.

If life had been spared him, Dr. Cannon would have worked ceaselessly for the Spanish outcasts in France, and he would have been sympathetic towards aiding a hospital to lighten their misery. He was always intimately involved with actual medicine and surgery, and for years the staff of the Peter Bent Brigham Hospital felt his close interest in their problems. Moreover, throughout World War I all his efforts while he was in France and England were directed toward solution of the clinical problems represented by surgical shock and hemorrhage. In World War II his interests continued in the same direction and were coupled with efforts to promote more intimate relations between productive scholars in different countries.

The memorial is finely appropriate to the man and he in his turn would have been particularly happy that this just and merciful monument in his name is, at least in part, the gift of medical friends and colleagues. Many will remember how touched he was on the occasion of his twenty-fifth year at George Higginson Professor of Physiology, Harvard Medical School, that the funds for the celebration were subscribed in small amounts from several hundred former students and associates, and not in large contributions from a few. It is to be hoped that men and women in medicine will respond to this appeal by giving what they can. Good wishes mean much, but a good wish with a single dollar behind it can mean much more!

## THE CARE OF THE PATIENT

WE have become accustomed, in recent years, to think of the care of the patient from an economic and sociologic point of view — to fall in line with the theory, not now so startling as it once was, that the inhabitants of the earth should share more freely than was once the case in the fruits of their earth and in the benefits of human progress. From the tradition cherished at one time that the patient was a sort of bond servant of his practitioner, because of his own choice, we are gradually coming to entertain the idea that reasonably good medical care should be available, at least to most of us, at a price commensurate with our ability to pay, and that that cost, in fairness to the profession supply-

ing the service, should be spread over the whole population or certain segments of it

Thus have come into being prepaid hospital-insurance plans, group practice as applied to industries, respectable coalitions of physicians to furnish medical service at a reasonable cost, as exemplified by the Blue Shield of the Massachusetts Medical Society, and, finally, impending federal

control of certain types or parts of practice. This does not necessarily spell the doom of all private practice as we have known it, with its inadequacies and its inequalities both as to cost and as to quality, but it does mean that a social revolution is on the high road, and we might as well ride with it.

Many of these things will come to pass well or ill, wisely or unwisely, according to the will of

the people and the ability of their representatives to plan, and since we cannot block them we had best try and direct them. What concerns us even more closely, because it is our medical skill that provides it, is the caliber of care that our fellow men receive from us. This we must not lose sight of when we are arguing over costs because we, and not the patient, know best the quality of our goods.

It is, of course, a truism to say that medical knowledge and the treatment and prevention of disease, which are the aims of medical knowledge, are making rapid advances. They have been making rapid advances since the authority of Galen was thrown off. What is important to recognize is that the art of medicine, valuable as it is, is becoming more and more simply an adjunct of the science. More and more the study and the treatment of the sick are being taken away from the home and the office and brought into the hospital and its contiguous laboratory.

Less and less is the practitioner — and this is no reflection on him — able alone to carry out the

studies and institute the treatments that his patients may require. Hospital facilities must be available to him, but whether or not he is on the staff, those facilities are usually inadequate unless they include trained professional personnel — in the operating rooms, in the x-ray department, in the laboratory and on the ward.

Much of the best medical care now depends on

teamwork, — this is the real revolution in medicine, — and this often implies the best hospital care in every sense of the word. One of the crying needs of medical practice today, so far as the technical care of the patient is concerned, is not simply to have a hospital to which the practitioner can take his patient and there care for him but rather to have a hospital to which he can take him and, if

necessary, leave him to the care of those qualified in the details of modern medical procedures.

### MASSACHUSETTS MEDICAL SOCIETY POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to

George L. Schadt, *Chairman*  
Postwar Loan Fund  
8 Fenway  
Boston 15, Massachusetts

### MASSACHUSETTS MEDICAL SOCIETY DEATHS

ELLIS — Edward K. Ellis, M.D., of Needham, died June 7. He was in his sixty-seventh year.

Dr. Ellis received his degree from Tufts College Medical School in 1902. He was a member of the New England Ophthalmological Society and a fellow of the American Medical Association.

His widow survives.

OVERLANDER — J. Eliot Overlander, M.D., of Springfield, died May 26. He was in his sixty-sixth year.

Dr. Overlander received his degree from Harvard Medical School in 1909. He was formerly senior medical officer of the Springfield Hospital. He was a fellow of the American Medical Association.

His widow survives.

QUEST — James F. Quest, M.D., of Boston, died May 27. He was in his sixty-eighth year.

Dr. Quest received his degree from the University of Vermont College of Medicine in 1906. He was a fellow of the American Medical Association.

TREANOR — John P. Treanor, M.D., of Dorchester, died May 4. He was in his eighty-second year.

Dr. Treanor received his degree from Harvard Medical School in 1895. He was a member of the New England Pediatric Society and a fellow of the American Medical Association.

His widow survives.

## MISCELLANY

DR WALTER B CANNON MEMORIAL  
HOSPITAL FUND

A memorial to Dr Walter B Cannon, late George Higginson Professor of Physiology at Harvard Medical School, is to be established in Toulouse, France. A hospital there, organized and staffed by Spanish refugees in France to serve their fellow refugees, is to be expanded and operated under its new name, the Dr Walter B Cannon Memorial Hospital.

Dr Cannon, who was president of the American Association for the Advancement of Science in 1939, actively aided the Spanish Republicans from the start of the Civil War in 1936 to the end of his life. He became chairman of the Medical Bureau to Aid Spanish Democracy in 1937 and at his death was honorary co-chairman, Boston Chapter, Joint Anti-Fascist Refugee Committee. Through the Unitarian Service Committee, the Joint Anti-Fascist Refugee Committee has been helping 150,000 Spanish refugees remaining in France after three years of war and seven years of destitution and suffering. Ineligible for aid from the Red Cross, UNRRA or the French Government, these people without a country are as acutely in need of medical care as almost anyone in the world. They depend entirely on American charity.

About one hundred and fifty prominent Boston citizens have just started a drive for \$75,000 to buy some of the necessary equipment for the hospital in Toulouse and to safeguard its continued operation. All funds are managed and spent in France by the Unitarian Service Committee. After Spain returns to democracy, the memorial to Dr Cannon will be perpetuated there.

Co-chairmen of the drive are Dr George R. Minot, professor of medicine, Harvard Medical School, Dr Frederick May Eliot, president, American Unitarian Association, Ralph Barton Perry, professor of philosophy, Harvard University, and Paul T. Smith, attorney. Among the medical sponsors are Drs Donald G. Anderson, Joseph C. Aub, Herrman L. Blumgart, Arlie V. Bock, Ethan Allan Brown, Allan M. Butler, William B. Castle, David Cheever, Stanley Cobb, Edwin J. Cohn, Hilbert F. Day, Robert L. DeNormandie, Cecil K. Drinker, John T. Edsall, Laurence B. Ellis, James M. Faulkner, Jacob Fine, Alexander Forbes, Channing Frothingham, James L. Gamble, Bernard I. Goldberg, Charles A. Janeway, Chester S. Keefer, Mary R. Lakeman, Eugene M. Landis, Samuel A. Levine, Moses H. Lurie, Helen I. D. McGillicuddy, J. H. Means, Leroy M. S. Miner, Dwight O'Hara, Marian C. Putnam, David Rapoport, George C. Shattuck, Richard M. Smith, Paul D. White, George B. Wislocki and S. Burt Wolbach.

Headquarters of the Dr Walter B. Cannon Memorial Hospital Fund are at 14 Beacon Street, Boston.

## CORRESPONDENCE

## FIRST USE OF X-RAYS IN BOSTON

*To the Editor* The letter in the May 16 issue of the *Journal* on the first use of x-rays in Boston reminded me of an incident. As a student I sat in the staff chairs of the old amphitheater at the Massachusetts General Hospital waiting for Dr Warren's lecture and reading the *Boston Post*, in which there was a short item mentioning that a Doctor Roentgen, of Vienna, had discovered a method of photographing the bones through the flesh. I circled it with a blue pencil and passed it to Dr Warren when he came in. He read it and smiled, remarking, "That is a good newspaper story, isn't it, young man?" Before many months Dr Warren was having his own cases x-rayed. I never got a chance to remind him of his remark.

Walter Dodd, who was the Massachusetts General Hospital pharmacist and who was interested in photography, took many pictures of pathological specimens. Being a snapshot amateur, I was interested in his work. In fear and trembling I got a picture of the dissecting room in the Boylston Street Medical School, and was caught by good old Tom Bonney, but gave him a print to placate him. Fond memories.

PHILIP C. MEANS, M.D.

Merrimac, Massachusetts

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*Periodontal Diseases and Soft Tissue Lesions of the Oral Cavity. Diagnosis and treatment.* By Arthur H. Merrett, D.D.S., Sc.D. Third edition. 8°, cloth, 256 pp., with 53 illustrations. New York: Macmillan Company, 1945. \$3.50.

† The previous editions of this monograph contained only the text on periodontal diseases. In this third edition a second part, comprising six chapters on soft-tissue lesions of the mouth, has been added. The author's approach is clinical, and the original text has been revised and brought up to date.

*A Textbook of Ophthalmology.* By Sanford R. Gifford, M.D. 12°, cloth, 457 pp., with 215 illustrations, 4 charts and 13 plates. Philadelphia: W. B. Saunders Company, 1945. \$4.00.

Dr Gifford before his death completed the revision of the third edition of his small textbook first published in 1938. The text has been brought up to date, and new material has been added on ptosis, contact glasses, cyclodiathermy and keratoconjunctivitis. New illustrations in black and white have been incorporated in the text. Also twelve full page color plates are used to delineate common diseased conditions of the eyes. The objective of the author, formerly professor at Northwestern University, was to compress into a small volume for medical students and general practitioners the essentials of modern ophthalmology. The need for three editions of his book speaks well for the attainment of his purpose.

## NOTICES

## SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JUNE 27

FRIDAY, JUNE 28  
\*10:00 a.m.-12:00 p.m. Medical Staff Rounds. Peter Bent Brigham Hospital.

TUESDAY, JULY 2  
\*12:15-1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, JULY 3  
\*10:30-11:30 a.m. Medical Clinic. Isolation Building Amphitheater, Children's Hospital.

\*12:00 p.m. Clinicopathological Conference (Children's Hospital) Amphitheater. Peter Bent Brigham Hospital.

\*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

\*Open to the medical profession.

MARCH 15-SEPTEMBER 15. Boston University Course for Discharged Medical Officers. Page 240, issue of February 14.

JUNE 20-22. American Association for the Study of Goiter. Page 312, issue of February 28.

JUNE 29. American College of Chest Physicians. Page 544, issue of April 18.

JULY 3. Harvard Medical Alumni Association. Page 603, issue of June 13.

SEPTEMBER 4-7. American Congress of Physical Medicine. Page 616, issue of May 2.

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## DISPUTED INDICATIONS AND TECHNICS FOR CESAREAN SECTION\*

EDWARD G. WATERS, M.D.†

JERSEY CITY, NEW JERSEY

WITH cesarean section, opinion on indications and choice of operation should certainly approach unanimity. So much has been written and so many formidable analytic compilations have been advanced that one might well doubt that serious divergence of opinion would exist concerning any factor of importance bearing on cesarean section. This happy state can hardly be considered to have arrived, however, if one but scans the more recent publications.

Our clinic is somewhat unusual in the interrelations of its three services. Each admits patients for a twenty-four-hour period in rotation, and the conduct of complicated labor is the responsibility of the chief of service. This arrangement has encouraged lively dispute and discussion through the years, unrestrained yet honest, open and constructive. As a result of constant reappraisal of results in open meetings shared by the three services, settled opinions have been recorded. Thus, after fourteen years and over 30,000 deliveries, we find ourselves largely in agreement on the indications for cesarean section, as well as on the technics to be followed.

We recognize that not all would agree with our attitude toward these problems. It is the purpose of this paper to discuss the most frequently disputed indications and to state the position currently arrived at with respect to them and to the operations preferred.

### INDICATIONS

The first problem is that of elective cesarean section for primiparas. One might immediately ask who elects and on what foundation. With cases of obvious fetopelvic disproportion there is no dispute. These, however, form a distinct minor group. The vast majority of cases constitute the so-called "borderline pelvis" group, in which the estimation of the fetopelvic relation establishes a challenge to the most honest and capable attendant in his effort to determine the proper solution. We frankly admit

our inability in many such cases to decide in advance of an adequate test of labor the ability of the patient to deliver herself or to be safely delivered by vagina. We marvel at the judgment and experience of the omniscient, which permit *in advance of labor* appreciation of the size, shape and moldability of the fetal head, the extent of the physiologic relaxation of the pelvic joints, the thickness and tension of the nonosseous pelvic structures, the character and effectiveness of the uterine contractions, the time factor in even partial dilatation and effacement of the cervix, the exact expectation date and the favorable parturitional effect that the unknown, possibly endocrine instigator of labor may exert. Certainly mechanical and x-ray pelvimetry, no matter how accurate, tell none of these things.

With due regard for these factors, we allow sufficient labor in borderline pelvic cases to permit the primiparous patient to demonstrate her capability for vaginal delivery. In patients with premature rupture of the membranes who go into labor late or are seen after what we consider a safe period for a clean operation, with a proper operational armamentarium there is surely no urgency until labor advances. The majority may be expected to progress as if such membrane rupture had not occurred, and the problematical status of the minority puts them in a group for special management in any case. Not many of us now accept premature rupture of the membranes per se as an indication for cesarean section, even when the exact fetopelvic estimation is not clear. We regard x-ray pelvimetry with esteem but without abject deference and place it well below the clinical examination and estimation of the patient's labor prospects. These opinions direct a policy of allowing all primiparas adequate labor except in the presence of obvious disproportion when labor begins.

The role of cesarean section in cardiac patients was formerly highly debatable. We no longer perform it in these cases unless there is an obstetric indication for the operation. Nor do we permit its use solely for the purpose of sterilization, when there are other methods that are so much easier. Between

\*From the Margaret Hague Memorial Hospital.  
†Associate Professor of Obstetrics and Gynecology, Columbia University.

## MISCELLANY

### DR WALTER B CANNON MEMORIAL HOSPITAL FUND

A memorial to Dr. Walter B. Cannon, late George Higginson Professor of Physiology at Harvard Medical School, is to be established in Toulouse, France. A hospital there, organized and staffed by Spanish refugees in France to serve their fellow refugees, is to be expanded and operated under its new name, the Dr. Walter B. Cannon Memorial Hospital.

Dr. Cannon, who was president of the American Association for the Advancement of Science in 1939, actively aided the Spanish Republicans from the start of the Civil War in 1936 to the end of his life. He became chairman of the Medical Bureau to Aid Spanish Democracy in 1937 and at his death was honorary co-chairman, Boston Chapter, Joint Anti-Fascist Refugee Committee. Through the Unitarian Service Committee, the Joint Anti-Fascist Refugee Committee has been helping 150,000 Spanish refugees remaining in France after three years of war and seven years of destitution and suffering. Ineligible for aid from the Red Cross, UNRRA or the French Government, these people without a country are as acutely in need of medical care as almost anyone in the world. They depend entirely on American charity.

About one hundred and fifty prominent Boston citizens have just started a drive for \$75,000 to buy some of the necessary equipment for the hospital in Toulouse and to safeguard its continued operation. All funds are managed and spent in France by the Unitarian Service Committee. After Spain returns to democracy, the memorial to Dr. Cannon will be perpetuated there.

Co-chairmen of the drive are Dr. George R. Minot, professor of medicine, Harvard Medical School, Dr. Frederick May Eliot, president, American Unitarian Association, Ralph Barton Perry, professor of philosophy, Harvard University, and Paul T. Smith, attorney. Among the medical sponsors are Drs. Donald G. Anderson, Joseph C. Aub, Herrman L. Blumgart, Arlie V. Bock, Ethan Allan Brown, Allan M. Butler, William B. Castle, David Cheever, Stanley Cobb, Edwin J. Cohn, Hilbert F. Day, Robert L. DeNormandie, Cecil K. Drinker, John T. Edsall, Laurence B. Ellis, James M. Faulkner, Jacob Fine, Alexander Forbes, Channing Frothingham, James L. Gamble, Bernard I. Goldberg, Charles A. Janeway, Chester S. Keefer, Mary R. Lakeman, Eugene M. Landis, Samuel A. Levine, Moses H. Lurie, Helen I. D. McGillicuddy, J. H. Means, Leroy M. S. Miner, Dwight O'Hara, Marian C. Putnam, David Rapport, George C. Shattuck, Richard M. Smith, Paul D. White, George B. Wislocki and S. Burt Wolbach.

Headquarters of the Dr. Walter B. Cannon Memorial Hospital Fund are at 14 Beacon Street, Boston.

## CORRESPONDENCE

### FIRST USE OF X-RAYS IN BOSTON

To the Editor: The letter in the May 16 issue of the *Journal* on the first use of x-rays in Boston reminded me of an incident. As a student I sat in the staff chairs of the old amphitheater at the Massachusetts General Hospital waiting for Dr. Warren's lecture and reading the *Boston Post*, in which there was a short item mentioning that a Doctor Roentgen, of Vienna, had discovered a method of photographing the bones through the flesh. I circled it with a blue pencil and passed it to Dr. Warren when he came in. He read it and smiled, remarking, "That is a good newspaper story, isn't it, young man?" Before many months Dr. Warren was having his own cases x-rayed. I never got a chance to remind him of his remark.

Walter Dodd, who was the Massachusetts General Hospital pharmacist and who was interested in photography, took many pictures of pathological specimens. Being a snapshot amateur, I was interested in his work. In fear and trembling I got a picture of the dissecting room in the Boylston Street Medical School, and was caught by good old Tom Bonney, but gave him a print to placate him. Fond memories.

PHILIP C. MEANS, M.D.

Merrimac, Massachusetts

## BOOKS RECEIVED

The receipt of the following books is acknowledged and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear of particular interest will be reviewed as space permit. Additional information in regard to all listed books will be gladly furnished on request.

*Periodontal Diseases and Soft Tissue Lesions of the Oral Cavity: Diagnosis and treatment.* By Arthur H. Merritt, D.D.S. Sc.D. Third edition. 8°, cloth, 256 pp., with 53 illustrations. New York: Macmillan Company, 1945. \$3.50.

The previous editions of this monograph contained on the text on periodontal diseases. In this third edition, second part, comprising six chapters on soft-tissue lesions of the mouth, has been added. The author's approach, clinical, and the original text has been revised and brought up to date.

*A Textbook of Ophthalmology.* By Sanford R. Gifford, M.D. 12°, cloth, 457 pp., with 215 illustrations, 4 charts and 1 plate. Philadelphia: W. B. Saunders Company, 1944. \$4.00.

Dr. Gifford before his death completed the revision of the third edition of his small textbook first published in 1933. The text has been brought up to date, and new material has been added on ptosis, contact glasses, cyclodiatheism and keratoconjunctivitis. New illustrations in black and white have been incorporated in the text. Also twelve full page color plates are used to delineate common disease conditions of the eyes. The objective of the author, formerly professor at Northwestern University, was to compress into a small volume for medical students and general practitioners the essentials of modern ophthalmology. The need for three editions of his book speaks well for the attainment of his purpose.

## NOTICES

### SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JUNE 27

FRIDAY, JUNE 28  
\*10:00 a.m.-12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

TUESDAY, JULY 2  
\*12:15-1:15 p.m. Clinicorontogenological Conference. Peter Bent Brigham Hospital.

WEDNESDAY, JULY 3  
\*10:30-11:30 a.m. Medical Clinic. Isolation Building Amphitheater. Children's Hospital.

\*12:00 m. Clinicopathological Conference. (Children's Hospital Amphitheater. Peter Bent Brigham Hospital).

\*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater. Children's Hospital.

\*Open to the medical profession.

MARCH 15-SEPTEMBER 15. Boston University Course for Discharge Medical Officers. Page 240. Issue of February 14.

JUNE 20-22. American Association for the Study of Goiter. Page 312. Issue of February 28.

JUNE 29. American College of Chest Physicians. Page 544, issue of April 18.

JULY 3. Harvard Medical Alumni Association. Page 803, issue of June 13.

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It was believed that a hysterectomy would be fatal, for the contraction of the uterus permitted further blood loss and the reappearance of shock. A procedure that I have found life-saving in similar cases was therefore performed. The loose peritoneum at the lateral edges of the incision was dissected to expose the uterine arteries, and these were ligated — but not cut — with ties of No. 2 chromic catgut. Within a few minutes the flabby noncontracting uterus exhibited fibrillary contractions and assumed the crinkled or crepe-paper appearance that indicates response to the induced anoxia.

The intravenous administration of blood, maintenance of the Trendelenburg position, the application of heat and so forth were continued. Four hours postoperatively the pulse was 90 and of good quality and the blood pressure was 124/90. The patient had almost complete anuria for 3 days but thereafter made an uneventful convalescence. There were some residual signs indicating damage to the cerebral nerve tissue from shock-anoxia, but these have since cleared up.

In view of the existing lesions, this patient would probably have succumbed if temporizing measures had been employed.

Our attitude toward pre-eclampsia and eclampsia is definitely conservative. We do not perform cesarean section on patients with eclampsia unless antitoxic measures have checked the eclampsia and made the patient operable. Patients with pre-eclampsia are treated medically unless the toxemia is progressive or recurrent. Termination of the pregnancy is then proceeded with, for we have found that the old practice of carrying the patient along has produced poor results in morbidity and mortality for mother and baby alike. Chesley's<sup>2</sup> follow-up of our patients shows the earlier the onset of toxemia and the longer it obtains before delivery, the poorer the prognosis for the baby and the worse the end result for the mother. Babies delivered early in a severely toxemic pregnancy have a better chance than those carried to or near term, and permanent damage to maternal structures parallels the duration of the toxemia. The method of terminating the pregnancy is dependent on the severity of the toxemia and associated factors, such as abruption.

Data on 879 cases of mild pre-eclampsia have been recorded. There were no maternal deaths. These cover a five-year period ending in 1940. Cesarean section was performed in 61 cases (6.9 per cent), an incidence approximately twice the clinic incidence. Approximately two thirds of the operations were performed because of fetopelvic disproportion. There were 16 cases of abruption, and in 5 of these cesarean section was performed, with 4 stillbirths.

In 117 cases of severe pre-eclampsia seen during the same period, section was done in 26 (22 per cent). Eleven patients had abruption of the placenta, 4 had cephalopelvic disproportion and 11 had other complications as coexisting indications. The need for cesarean section in severe pre-eclampsia is thus seen to be three times as great as it is in the mild group. The operative mortality was 8 per cent, 2 deaths ensuing when abruption of the placenta complicated the severe toxemia. There were 5 deaths in all, — a mortality of 4 per cent, — 4 of them in patients with abruption of the placenta. Since 78 per cent of those with severe pre-eclampsia were delivered vaginally, it is evident that our policy is

to treat all such cases energetically and anticipate vaginal delivery but to resort to cesarean section when progressive or recurrent toxemia is present and in some cases with placental abruption. Section was performed in 11 of 17 patients with abruption occurring with severe toxemia, with 2 deaths. In 6 cases in which the patients were allowed to deliver vaginally, there were 2 deaths. In all 17 cases the infants were stillborn.

From 1931 until November, 1945, we treated 236 cases of eclampsia. Nineteen patients died, a mortality of 8 per cent, and 10 were undelivered. Cesarean section was performed in 20 cases (8 per cent), in 4 of them for severe abruption. In 5 cases section was done on patients with severe toxemia who developed eclampsia post partum, in 15 cases it was done on eclamptic patients. Two patients were operated on while uncontrolled, in opposition to the practice in our clinic. Section was performed in 10 cases one to nine days after the initial convulsion, and in 3 on the day of the first convulsion because of severe placental abruption. There were no maternal deaths following any of the cesarean sections. With elimination of the 5 cases in which eclampsia developed postoperatively, the patients having been progressively pre-eclamptic when operated on, and the 3 cases in which operation was performed for abruption complicating eclampsia, the corrected incidence of cesarean section in eclampsia is seen to be 12, or 5 instead of 8 per cent. This figure clearly indicates our present attitude toward cesarean section in eclampsia. The operation is not employed if we know or believe that the patient is about to have convulsions. It is occasionally done when the convulsive phase has been completely overcome. It is sometimes necessary when abruption of the placenta occurs. But eclampsia should be one of the rarest indications. If it is employed in the convulsive stage, a high mortality, such as that reported by De Normandie<sup>3</sup> in his last five-year study — 21 per cent of 53 cases — may be anticipated.

From October, 1931, through 1944, we observed 215 known hypertensive patients who went through two hundred and seventy pregnancies. There were 6 maternal deaths, a mortality of 2 per cent. In two hundred and thirteen pregnancies carried past twenty-eight weeks, cesarean section was performed in 28 cases and hysterotomy in 3 of these, with 1 maternal death — a mortality of 4 per cent — and 7 fetal deaths — a mortality of 25 per cent. In one hundred and eighty-five vaginal deliveries, the corresponding mortality rates were 1 and 24 per cent. Two patients died undelivered, and 1 after an abortion at twenty-three weeks. There were 15 cases of abruption, with a total loss of 80 per cent. Eleven patients were delivered vaginally, with no deaths, and on 4 cesarean section was performed, with 1 death due to peritonitis.

January, 1933, and August, 1942, in a series of 578 cases of cardiac disease complicating pregnancy 39 (6.7 per cent) were subjected to cesarean section. The operative incidence, however, dropped from 8 per cent in the first 345 cases to 4.4 per cent in the last 223 cases, with a clinic incidence of 1.3 per cent as compared with one of 15 per cent among 53 private patients.<sup>1</sup>

We employ a system of absolute bed rest for patients who have had or are threatened with decompensation, and constant cardiologic supervision for all the seemingly less severe cardiac cases. In this group, the incidence of decompensation has been reduced from 22.3 to 2.5 per cent and the mortality from 3.5 to 0.6 per cent, largely through competent medical care and the elimination of operative interference except for strictly coincidental obstetric indications. Such appraisal of experiences supports our proscription of cesarean section on purely cardiac indications, for private and clinic patients alike. The management and conduct of the cardiac patient in labor is determined by the cardiac consultant and the chief of service.

There are few conditions that have aroused more debate on management than has abruption of the placenta or premature separation of the placenta after the twenty-eighth week of pregnancy. We all recognize the occurrence of slight or partial separations that present no clinical problem. We admit the value of early diagnosis of mild cases, especially

cesarean section in a multiparous patient with an effaced cervix approaching full dilatation in whom an abruption develops or in any patient with shock or hemorrhage, without first re-establishing

TABLE 2 *Maternal Mortality in Severe Cases of Abruptio*

DELIVERY	NO OF CASES	NO OF DEATHS	MORTALITY %
Vaginal	38	2	5
Cesarean section	50	2	4
Totals	88	4	

blood volume, overcoming anoxia and combating shock? Who would refuse this operation when a complete abruption occurs with the cervix and birth tract unready for delivery, when means are readily at hand for combating shock and blood loss? Who dares sit by while an initial response to active measures against shock may cloak disruption of the myometrium and progressive hemorrhage into the broad ligaments and peritoneal cavity? The answers fix the policy of the clinic, and the validity of such answers is to be found in the mortality report. Injudicious or poor management means more deaths, and there is no statistical compromise with death. On this basis and on that of the data on our material already published we are willing to be judged.

A brief recital of an extremely severe case, illustrating sequential procedures, follows.

A 40-year-old multigravida was seen on February 21, 1945, about 2 weeks beyond term, in deep shock. The prenatal course had been normal, and there had been no abnormal or toxemic findings 5 and 2 days previously.

The patient fainted in her home and remained unconscious for 8 minutes. There were no other signs or symptoms. A relative, a competent obstetrician, examined her within 15 minutes. At that time she was mentally clear. The blood pressure was 120/60 and the pulse 78, the uterus was relaxed, and the fetal heart beat was present. Since the patient was at or beyond term and had never fainted before, she was sent to the hospital for the purpose of inducing labor.

Half an hour after admission, the patient was in deep shock, with a blood pressure of 64/20 and a pulse of 70, barely palpable, cold wet extremities and poor vascular tone. There was some abdominal tenderness but no pain, and the uterus seemed to have considerably increased in size in 5 days. She became unconscious and almost moribund, no pulse or blood pressure being obtainable. The fetal heart could not be heard.

Intravenous injections of plasma were begun at once and, while bank blood was being cross-matched, glucose solution was concurrently run into the other arm. In 2 hours, forced administration of 750 cc of plasma, 1000 cc of blood and 1000 cc of 10 per cent glucose, together with the administration of oxygen and the usual measures against shock, caused a rise in the blood pressure to 110/70 and a good pulse of 88. The patient regained consciousness, felt well and took an active interest in the proceedings, although she had received 0.03 gm of morphine. There was still no vaginal bleeding. The abdomen was opened and a hugely distended Couvelaire type of uterus was revealed. The lower segment was markedly stretched, and when incised spouted blood to a height of 1 meter. A rapid low transverse cesarean section was done, and the dead fetus, huge clots and the separated placenta were removed. The uterine incision was closed, but the uterus failed to contract under stimulation or the intravenous and intra-uterine injection of oxytocics.

TABLE 1 *Methods of Delivery in Abruptio*

METHOD	MILD CASES		SEVERE CASES	
	NO	PER CENTAGE	NO	PER CENTAGE
Spontaneous	63	43	20	23
Low forceps	30	20	4	5
Midforceps	8		2	
Bagging	5		7	
Version	4		1	
Breech extraction	16		1	
Artificial rupture of membranes	3		2	
Packing of cervix or uterus	1		1	
Cesarean section		12		56
Classic	3		11	
Low vertical	3		11	
Low transverse	12		28	
Porro	0		0	
Totals	148		88	

in toxemic and primiparous patients, which may presently progress to the severest form. Most of us are not misled by the amount of external blood loss usually noted in over 80 per cent of mild and severe cases alike. The degree of shock is dependent on myometrial disruption as well as on blood loss, and it is frequently difficult to know which of these is more responsible for associated symptoms. If one admits the existence of the mild, the progressive and finally the complete abruption, with its dramatic picture and disastrous possibilities, one must also agree that each presents its own problem and requires its own solution. Who would perform



It was believed that a hysterectomy would be fatal, for the retraction of the uterus permitted further blood loss and the reappearance of shock. A procedure that I have found effective in similar cases was therefore performed. The loose peritoneum at the lateral edges of the incision was dissected to expose the uterine arteries, and these were ligated—but not cut—with ties of No. 2 chromic catgut. Within a few minutes the flabby, noncontracting uterus exhibited fibrillary contractions and assumed the crinkled or crepe-paper appearance that indicates response to the induced anoxia.

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Packing of cervix or uterus	1		1	
Cesarean section		12		56
Classic	3		11	
Low vertical	3		11	
Low transverse	12		28	
Porro	0		0	
Totals	148		88	

in toxemic and primiparous patients, which may presently progress to the severest form. Most of us are not misled by the amount of external blood loss usually noted in over 80 per cent of mild and severe cases alike. The degree of shock is dependent on myometrial disruption as well as on blood loss, and it is frequently difficult to know which of these is more responsible for associated symptoms. If one admits the existence of the mild, the progressive and finally the complete abruption, with its dramatic picture and disastrous possibilities, one must also agree that each presents its own problem and requires its own solution. Who would perform

were so. The uterus at term is an organ well protected by nature to withstand infection, else most women would die. Its excellent blood supply, the diminished lymphatic and venous drainage with post-parturient contraction, the return to pelvic location early in involution, late cervical contraction with adequate external drainage and the increase at term of the natural resistance to bacterial invasion all indicate control of uterine infection if no peritonitis has been induced. Patients with foul intrauterine infections do not die either after extraperitoneal cesarean section or after eventual delivery by vagina. But if they have had a classic or low-segment cesarean section they often do, and peritonitis kills most of those dying after Porro operations. The surgeon who performs a Porro operation always assumes that without it the patient would have died, but with an extraperitoneal operation the patient would have recovered in any case. The figures from appreciable groups of cases could be allowed to speak for themselves, without "correcting" for certain deaths. We no longer believe that patients die from myometritis, parametritis or pelvic cellulitis provided that the infected areas are drained, but they still die from peritonitis. In

all septic parturient patients, the peritoneal cavity should not be opened. How better can one obey than with an extraperitoneal cesarean section? And except for vaginal delivery, there is no other way.

The operation in itself is an anatomical one of moderate difficulty but certainly presents no challenge to the obstetrician of surgical competence. The second-time hernia operation by the anatomy-wise and adept intern is generally a creditable one. The same can be said for the extraperitoneal operation. Either the paravesical (Latzko) or the supra-vesical (Waters) approach is good, with definite advantages favoring the latter. The majority of operations in our clinic are now performed with this technic.

39 Gifford Avenue

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### THE TREATMENT OF BACTERIAL ARTHRITIS WITH PENICILLIN\*

HAROLD L. HIRSH, M.D.,† HENRY L. FEFFER, M.D.,‡ AND HARRY F. DOWLING, M.D.§

WASHINGTON, D. C.

UNTIL the discovery of penicillin, the methods of treating the infectious arthritides were not entirely satisfactory. Although the sulfonamides were often valuable, the results obtained with them left much to be desired. The superior antibacterial action of penicillin in vitro justified a trial of this agent in certain bacterial infections of the joints. The present report is an account of our experience with penicillin in the treatment of 26 patients with bacterial arthritis.

#### GNOCOCCAL ARTHRITIS

Seventeen patients with gonococcal arthritis were treated with penicillin (Table 1). The diagnosis was made in 9 cases by culturing gonococci from the joint fluid and in 8 cases by finding gram-negative diplococci in a smear of the joint fluid. Thirteen of the patients also exhibited a local genital or urinary infection from which gonococci were cultured or which showed gram-negative diplococci on smear. There were 9 men and 8 women. In 15 cases the

arthritis was acute, having been present for less than a month in each. In the remaining 2 patients the disease had been present for three and six months, respectively.

The patients with acute gonococcal arthritis may be divided into two groups according to the kind of treatment received. The 7 patients in Group A were given penicillin intramuscularly for short periods, ranging from eight to thirty hours. One patient (Case 3) was given a second and a third course of intramuscular penicillin of seventy-two and one hundred hours' duration, respectively. Another patient (Case 6) received an injection of 50,000 units of penicillin intra-articularly, in addition to 80,000 units intramuscularly. A third patient (Case 7) was given 100,000 units of penicillin orally every two hours for forty-eight hours, followed by intermittent intramuscular injections to a total of 550,000 units. There was no improvement of the arthritis in any case, although local genitourinary infections, whenever present, cleared up completely. With the exception of 1 patient who left the hospital against advice, all these patients finally recovered on symptomatic measures, sulfonamides or fever therapy.

Because of the complete failure of these short courses of penicillin, it was decided to treat for at

\*From the George Washington Medical Division and the Orthopedic Service, Gallinger Municipal Hospital and the Department of Medicine, George Washington University.

†Fellow in medicine, George Washington University.

‡Formerly, resident in orthopedics, Gallinger Municipal Hospital.

§Clinical professor of medicine, George Washington University, chief George Washington Medical Division, Gallinger Municipal Hospital.

Another indication for cesarean section is placenta previa. Of 341 cases observed from January 1, 1932, through 1941, cesarean section was performed in 104, with no deaths. Among the 237 patients delivered vaginally there were 2 deaths.

### TECHNICS

In general, any type of cesarean section is relatively easy to perform. Previously it was largely in the hands of general surgeons, because most of those who delivered babies knew nothing about surgery. Although more adequate training in surgery and the application of surgical principles and technics have accelerated the surgical advance of obstetrics, too often there are adherence to old and outmoded procedures and hesitancy to utilize newer operations of proved worth. The surgical inferiority complex ill mantles the modern obstetrician; he must forget his midwife ancestry. He must be capable of successfully dealing with the technics and complications not only of any type of vaginal delivery but also of any type of abdominal delivery.

There are three major abdominal operations in obstetrics—transperitoneal section, extraperitoneal section and cesarean hysterectomy. The classic

Although the mortality figures for classic section and for the low-segment operation do not materially differ when done electively in good-risk patients not in labor and with intact membranes, the low-segment operation must be chosen for its lower morbidity, smoother convalescence and lessened incidence of subsequent rupture of the uterine scar. When the membranes have been ruptured or the patient has been long in labor or has been subjected to repeated examination, it is far superior. It is time for all obstetricians to learn and use an acceptable form of low-segment operation, and to cease justifying continued use of the antiquated classic section. Our own preference is for the low-segment operation with transverse cervical or isthmal incision. This means combining the old Kehrer technic with the Munro-Kerr incision placed low on the isthmal segment, as advocated and popularized by Phaneuf. In more than 2000 cesarean sections performed in this clinic during the last fourteen years, low-segment operations have been chosen in 69 per cent of cases (Table 3).

We believe that the Porro operation as employed in septic cases is an antiquated operation headed for the limbo of ancient and unused technics. Our

TABLE 3 Cesarean-Section Data (October 1, 1931, to January 1, 1945)

TYPE OF DELIVERY	NO. OF DELIVERIES	NO. OF DEATHS	MORTALITY	
			%	
All deliveries	75238	200	0.27	
Cesarean sections	2039	29	1.42	
Transperitoneal and exclusion	1406	13	0.92	
Extraperitoneal	483	5	1.03	
Waters's supravescical	290	2	0.6	
Latzko's paravescical	193	3	1.5	
Classic	121	8	6.6	
Hysterectomy (Porro)	28	3	10.7	
Vaginal	1	0		

operation is reserved for the last, when it precedes removal of the uterus. This applies to degenerating fibroids and those obstructing the birth canal, and uterine rupture. Using the classic operation rather than the low-segment operation in cases of placenta previa represents a poor conception of the anatomic relations of the placenta, uterus and blood supply. The major portion of a placenta previa is not located in the lower segment, and with transverse incision a lesser amount is incised. More positive suture control of the placental site is possible along the line of incision, and the thinner segment carries far fewer vessels. The uterine content and blood spill are kept out of the abdominal cavity, and more accurate estimation of blood loss is possible. The thin uterine wall is grasped with T clamps, and hemostasis is easily obtained while suturing proceeds. There is no valid reason for electing the classic operation in placenta previa, and in my opinion the low-segment operation is always better and safer.

experience with extraperitoneal operations during the last fourteen years shows a mortality rate far lower than that of comparable groups of Porro operations. It also indicates the needless sacrifice of uteri in Porro operations, and has caused us to reconsider our ideas on the manner of death in post-partum cesarean sepsis. The data from our clinic regarding extraperitoneal sections have recently been published<sup>4</sup> and will not be reviewed in detail. Septic deaths after section are usually due to peritonitis. In De Normandie's<sup>3</sup> last five-year report from Massachusetts, 39 per cent of the 273 deaths following cesarean section were from sepsis and another 10 per cent from embolus. There was a 4 per cent loss after extraperitoneal section. The hackneyed chant from the Porroites continually threatens us with the dire happenings that will follow retention of an infected uterus in the abdomen. This is voluble nonsense unsupported by facts. We could not possibly show a mortality of 1 per cent in over 500 cases of extraperitoneal section if this

were so The uterus at term is an organ well protected by nature to withstand infection, else most women would die Its excellent blood supply, the diminished lymphatic and venous drainage with post-parturitional contraction, the return to pelvic location early in involution, late cervical contraction with adequate external drainage and the increase at term of the natural resistance to bacterial invasion all indicate control of uterine infection if *no peritonitis has been induced* Patients with foul intrauterine infections do not die either after extraperitoneal cesarean section or after eventual delivery by vagina But if they have had a classic or low-segment cesarean section they often do, and peritonitis kills most of those dying after Porro operations The surgeon who performs a Porro operation always assumes that without it the patient would have died, but with an extraperitoneal operation the patient would have recovered in any case The figures from appreciable groups of cases should be allowed to speak for themselves, without "correcting" for certain deaths We no longer believe that patients die from myometritis, parametritis or pelvic cellulitis provided that the infected areas are drained, but they still die from peritonitis In

all septic parturient patients, the peritoneal cavity should not be opened How better can one obey than with an extraperitoneal cesarean section? And except for vaginal delivery, there is no other way

The operation in itself is an anatomical one of moderate difficulty but certainly presents no challenge to the obstetrician of surgical competence The second-time hernia operation by the anatomy-wise and adept intern is generally a creditable one The same can be said for the extraperitoneal operation Either the paravesical (Latzko) or the supravescical (Waters) approach is good, with definite advantages favoring the latter The majority of operations in our clinic are now performed with this technic

39 Gifford Avenue

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THE TREATMENT OF BACTERIAL ARTHRITIS WITH PENICILLIN\*

HAROLD L HIRSH, M D,† HENRY L FEFFER, M D,‡ AND HARRY F DOWLING, M D §

WASHINGTON, D C

UNTIL the discovery of penicillin, the methods of treating the infectious arthritides were not entirely satisfactory Although the sulfonamides were often valuable, the results obtained with them left much to be desired The superior antibacterial action of penicillin in vitro justified a trial of this agent in certain bacterial infections of the joints The present report is an account of our experience with penicillin in the treatment of 26 patients with bacterial arthritis

GONOCOCCAL ARTHRITIS

Seventeen patients with gonococcal arthritis were treated with penicillin (Table I) The diagnosis was made in 9 cases by culturing gonococci from the joint fluid and in 8 cases by finding gram-negative diplococci in a smear of the joint fluid Thirteen of the patients also exhibited a local genital or urinary infection from which gonococci were cultured or which showed gram-negative diplococci on smear There were 9 men and 8 women In 15 cases the

arthritis was acute, having been present for less than a month in each In the remaining 2 patients the disease had been present for three and six months, respectively

The patients with acute gonococcal arthritis may be divided into two groups according to the kind of treatment received The 7 patients in Group A were given penicillin intramuscularly for short periods, ranging from eight to thirty hours One patient (Case 3) was given a second and a third course of intramuscular penicillin of seventy-two and one hundred hours' duration, respectively Another patient (Case 6) received an injection of 50,000 units of penicillin intra-articularly, in addition to 80,000 units intramuscularly A third patient (Case 7) was given 100,000 units of penicillin orally every two hours for forty-eight hours, followed by intermittent intramuscular injections to a total of 550,000 units There was no improvement of the arthritis in any case, although local genitourinary infections, whenever present, cleared up completely With the exception of 1 patient who left the hospital against advice, all these patients finally recovered on symptomatic measures, sulfonamides or fever therapy

Because of the complete failure of these short courses of penicillin, it was decided to treat for at

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least five days all patients subsequently admitted. The 8 patients treated in this manner are listed in Group B. They were given amounts of penicillin totaling 925,000 to 2,000,000 units. In every case the symptoms and signs of joint disease completely subsided during the course of treatment and did not return. These patients have been kept under observation for periods varying from one to five months without any recurrence of their arthritis.

The 2 patients with chronic arthritis caused by the gonococcus were each given several short courses of penicillin. In addition, 1 was given three intra-

pneumococcus in 1 case each. Five of the 7 patients with staphylococcal arthritis recovered. Three of these were treated with intra-articular penicillin. The fourth (Case 21) received the drug by continuous intravenous administration. The fifth patient (Case 22) was given penicillin intramuscularly and when he failed to improve on this regime, supplemental intra-articular injections were employed. In Case 20, the joint healed following three injections of penicillin into the joint cavity, but the swelling and tenderness in the periarticular tissues improved more slowly and some induration and thick-

TABLE 1 *Results of Penicillin Treatment in Patients with Gonococcal Arthritis*

STATE OF DISEASE	CASE No.	AGE yr	SEX	RACE	No. OF JOINTS AFFECTED	GENITO-URINARY INFECTION	ROUTE OF ADMINISTRATION	DURATION OF TREATMENT	TOTAL DOSE units	RESULTS
Acute										
Group A	1	39	M	Negro	1	None	Intramuscular	8 hr	240 000	Unimproved
	2	23	F	Negro	2	None*	Intramuscular	12 hr	460 000	Unimproved
	3	22	M	Negro	2	Urethritis	Intramuscular	60 hr	500 000	Unimproved
								72 hr †	720 000	
								100 hr ‡	1,000 000	
	4	16	M	Negro	2	Urethritis	Intramuscular	16 hr	300 000	Unimproved
	5	33	M	White	1	Urethritis	Intramuscular	30 hr	300 000	Unimproved
	6	32	M	Negro	1	None	Intramuscular	8 hr	80 000	Unimproved
							Intra-articular	1 injection	50 000	
	7	28	M	Negro	3	Urethritis	Oral	48 hr	2 400 000	Unimproved
							Intramuscular	48 hr	550 000	
Group B	8	42	M	Negro	1	Urethritis	Intramuscular	5 days	925 000	Recovered
	9	20	F	Negro	1	Cervicitis and urethritis	Intramuscular	5 days	1 200 000	Recovered
							Intramuscular	5 days	1,200 000	Recovered
	10	25	F	Negro	1	Cervicitis and urethritis	Intramuscular	5 days	1,200 000	Recovered
	11	26	F	Negro	1	Cervicitis	Intramuscular	5 days	1 200 000	Recovered
	12	19	F	Negro	1	Cervicitis	Intramuscular	8 days	2 000 000	Recovered
	13	19	F	Negro	1	Cervicitis and urethritis	Intramuscular	8 days	2 000 000	Recovered
							Intramuscular	10 days	2 000 000	Recovered
	14	28	M	Negro	3	Urethritis	Intramuscular	10 days	2,000 000	Recovered
	15	19	F	Negro	2	Cervicitis and urethritis	Intramuscular	10 days	2,000 000	Recovered
Chronic	16	24	M	White	8	Urethritis	Intramuscular	12 hr	200 000	Unimproved
								8 hr	240 000	
								30 hr	300 000	
								40 hr	160 000	
							Intra-articular	3 injections	50 000	
									100 000	
									200 000	
									300 000	
	17	17	F	Negro	5	None*	Intramuscular	24 hr	300 000	Unimproved
								24 hr †	300 000	
								24 hr ‡	300 000	
								24 hr §	300 000	

\*Cervical erosion was present but gonococci could not be obtained on culture or smear.

†Second course.

‡Third course.

§Fourth course.

articular injections in amounts varying from 50,000 to 200,000 units. Although the urethritis that was present in 1 case subsided completely, the administration of penicillin had no effect on the condition of the joints in either patient. Both patients later received fever therapy in a hypertherm cabinet, with complete resolution of the arthritis.

#### STAPHYLOCOCCAL, STREPTOCOCCAL AND PNEUMOCOCCAL ARTHRITIS

Nine patients with other types of bacterial arthritis were treated with penicillin (Table 2). Staphylococci were isolated from the joint fluids in 7 cases and a hemolytic streptococcus and a Type 12

ening of these tissues remained. Two months later the swelling of these tissues increased, redness and heat reappeared, and a low-grade fever supervened. Penicillin administered intramuscularly resulted in a complete recovery within two weeks.

Both the patients with staphylococcal arthritis in whom penicillin therapy failed were treated at a time when the drug was scarce. Both had bacteremia as well as inflammation of a knee joint. One patient (Case 23) was given sulfamerazine by mouth and penicillin intra-articularly in daily injections of 50,000 units. Although penicillin concentrations of 0.156 to 0.625 units per cubic centimeter were maintained in the joint fluid—levels that were

found to be bactericidal for the patient's organism — staphylococci continued to be obtained on culture. The patient finally died of staphylococcal bacteremia

The other patient in whom treatment failed (Case 24) was given penicillin intramuscularly in doses of 20,000 units every four hours and in the knee joint in amounts of 10,000 units each day. Under this regime, the local bacteremia remained uncontrolled and the infection extended into the lower end of the femur, resulting in an osteomyelitis and periostitis. An arthrotomy was performed so that penicillin could be instilled into the joint through a catheter. When there was no improvement after this regime had been followed for three weeks, penicillin was

DISCUSSION

In view of the startling success of penicillin therapy in gonorrhea, one might expect similarly excellent results in acute arthritis caused by the gonococcus. Actually, the value of penicillin in the latter condition is an unsettled question at the present time. Thompson,<sup>1</sup> Bloomfield et al.<sup>2</sup> and Josey and Kirshman<sup>3</sup> obtained no benefit from the use of penicillin in their patients with gonococcal arthritis. On the other hand, some investigators<sup>4-11</sup> report excellent results in small series of patients. In some cases, the arthritis responded to a short course of penicillin administered for the primary genitourinary infection, whereas others required a longer course

TABLE 2 Results of Penicillin Treatment in Patients with Staphylococcal, Streptococcal and Pneumococcal Arthritis

CASE No	AGE	SEX	RACE	KNEE JOINT INVOLVED	ETIOLOGY	ROUTE OF ADMINISTRATION	DOSEAGE OF PENICILLIN	DURATION OF TREATMENT	RESULTS
	yr						units	days	
18	45	M	Negro	Left	Staphylococcus	Intra articular	20 000 daily	2	Recovered
19	7	F	Negro	Right	Staphylococcus aureus	Intra articular	2,500 twice daily 12,500 to 50 000 daily	10	Recovered
20	12	M	Negro	Right	Staphylococcus	Intra articular	30 000 to 80 000 every 3 days	5	Recovered*
21	36	M	Negro	Right	Staphylococcus	Intravenous	300 000 continuously	12	Recovered
22	29	M	Negro	Right	Hemolytic staphylococcus	Intramuscular Intra-articular	25 000 every 3 hr 50 000 every 2 days	14	Recovered†
23	54	F	Negro	Left	Hemolytic staphylococcus	Intra articular	50 000 daily	10	Died
24	22	F	Negro	Left	Hemolytic staphylococcus	Intra articular Intramuscular	10 000 daily 20 000 every 4 hr	16 28	Unimproved
25	33	M	Negro	Left	Beta hemolytic streptococcus	Intra articular  Intramuscular	50 000 to 200 000 every 2 to 3 days  100 000 to 200 000 continuously for 24 hr 15 000 every 3 hr	8  16	Recovered
26	29	M	Negro	Left	Pneumococcus Type 12	Intra articular	15 000 daily	21	Recovered

\*Two months later intramuscular penicillin was given for residual periarticular inflammation  
†Still receiving penicillin intramuscularly for possible acute tricuspid endocarditis.

discontinued. The joint was then placed in a cast, and the patient made a gradual but complete recovery.

One patient with arthritis of the left knee, caused by a beta-hemolytic streptococcus (Case 25) was given doses of penicillin varying from 50,000 to 200,000 units directly into the joint every second or third day over a period of eight days. Although the arthritis improved rapidly, swelling and tenderness of the periarticular tissues remained until penicillin was also administered intramuscularly, whereupon the entire infection healed completely.

A pneumococcal arthritis of the knee joint without any evidence of infection elsewhere was present in Case 26. At first, daily intra-articular injections of 15,000 units were administered. When improvement on this regime was incomplete, the dose was changed to 12,500 units twice per day. This was continued for fifteen days, by which time the patient had completely recovered.

or several courses. Most of these authors do not state whether there was swelling of the joints or other local signs of inflammation or whether the joint fluid contained leukocytes or bacteria.

The present study was confined to patients with an increased amount of fluid in one or more joints, which either yielded gonococci on culture or showed them on smear. The first 7 patients were given penicillin intramuscularly for periods of eight to thirty hours or, as in 1 case, orally for forty-eight hours. These regimes were uniformly unsuccessful, even though additional short courses of intramuscular penicillin were given to 2 patients and penicillin was injected into the knee joint of another. Since it was concluded that more prolonged treatment was necessary, each patient was given intramuscular injections approximating 10,000 units an hour for a period of at least five days. Of 8 patients so treated, improvement was not apparent for at least three days in 5 and not for five to eight days in 3. All

8 of the patients with acute arthritis treated by this method recovered completely

Our experience with chronic gonococcal arthritis has been limited. The 2 patients treated did not improve when given intramuscular penicillin, supplemented in 1 case by three intra-articular injections. In view of the results in patients with the acute form of the disease, better results might have been obtained in chronic arthritis if treatment had been extended over a longer period.

When one turns to the treatment of arthritis caused by the staphylococcus, streptococcus hemolyticus and pneumococcus, two principles are evident. First, penicillin should be injected into the joint in amounts and at intervals sufficient to provide a continuous bactericidal concentration. For the strains encountered we have found that doses of 50,000 units every second day or 100,000 units every third day are sufficient for this purpose. The second principle of treatment is that penicillin should be given systemically in adequate amounts and for long enough periods to combat extra-articular infection. It is probably best to administer it systemically to all patients for the first few days. In patients with bacteremia, inflammation of periarticular tissues or infections elsewhere in the body and in those who may be suspected of developing an osteomyelitis, systemic penicillin therapy should be continued until all evidences of infection have disappeared.

#### SUMMARY AND CONCLUSIONS

Twenty-six patients with bacterial arthritis were treated with penicillin. Seventeen of them had gonococcal arthritis, 7 had staphylococcal arthritis, and 1 each had arthritis caused by the hemolytic streptococcus and the pneumococcus.

Successful results were obtained in acute gonococcal arthritis when penicillin was administered

systemically in adequate doses, and in arthritis caused by the staphylococcus, the hemolytic streptococcus and the pneumococcus when adequate amounts of penicillin were injected into the joint, accompanied by penicillin systemically in patients with extra-articular infection.

The following dosage schedules are recommended. In acute gonococcal arthritis, 25,000 units should be injected intramuscularly every three hours for at least five days, or longer if needed. In arthritis caused by the staphylococcus, the beta-hemolytic streptococcus or the pneumococcus, 30,000 to 50,000 units should be administered intra-articularly on alternate days until local and general signs of inflammation have disappeared. If extra-articular infection is present, penicillin should also be given intramuscularly in amounts of 25,000 units every three hours.

2111 Bancroft Place, N W

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## THREE YEARS' EXPERIENCE WITH ELECTRIC CONVULSIVE THERAPY

JACOB NORMAN, M D,\* AND JOHN T SHEA, M D†

FOXBOROUGH, MASSACHUSETTS

**E**LECTRIC convulsive therapy has been used for the last three years at the Foxborough State Hospital and has become the chief form of physical therapy in the treatment of psychoses of psychogenic origin and of severe psychoneuroses. During this period 266 patients have been treated, as follows: schizophrenia, 175 cases, manic-depressive psychosis, 51 cases, involutional melancholia, 24 cases, and psychoneurosis, 16 cases. The majority of the schizophrenic patients had been in the hospital for periods ranging from one to thirty years and showed definite deterioration.

In all newly admitted functional cases, an attempt was made to obtain permission for shock therapy, especially in cases in which the patient presented serious difficulties in hospital care, such as combativeness, resistance to feeding, mutism, suicidal and homicidal tendencies and assaultiveness. Permission for treatment was readily obtained in 60 per cent of these cases.

During the first year of use of electric convulsive therapy, we tended to be conservative and in most cases waited two or three months before recommending the treatment. As time went on, experience convinced us that the time element is a great factor in the prognosis of shock therapy for schizophrenia and that the number of remissions proportionately decreases in relation to the length of illness. Of late it has been our policy to recommend this therapy early, and as a rule it is begun within thirty days following admission.

The criteria adopted for the selection of chronic cases for this treatment were rather broad. An attempt was made to obtain permission for treatment in cases that presented a syndrome of depression, agitation, guilt feelings and retardation, regardless of the diagnosis made. A large group of cases, most of which were those of chronic dementia praecox, were treated mainly because of requests coming from the patient's family, regardless of the duration of the illness and the type of onset. It is only during the last year that we have been reluctant to treat large numbers of old, deteriorated schizophrenic patients. Another group of chronic cases were selected for treatment because of the difficulties presented in their care, and the object was to modify symptoms to a point at which the patients would make a better hospital adjustment.

We have found that giving treatments three times weekly has met the therapeutic requirements for most patients. The number of treatments given

varied greatly. The acutely ill patients required a smaller number of treatments than did the chronic cases. The manic-depressive depressed and involutional melancholia cases required fewer treatments than did the manic-depressive manic cases. The schizophrenic patients in general required a larger number of treatments. In the treatment of chronic schizophrenic cases, we were governed by the reported experiences of Kalinowsky,<sup>1</sup> giving twenty treatments and, if improvement was evident, another series of ten to fifteen treatments after a rest interval of two or three weeks, even if the patient lost all the improvement gained from the first series. If no improvement was noted after the series of twenty treatments, no further treatment was given except that in 12 cases of chronic schizophrenia fifty treatments were given, regardless of the fact that the patients did not improve after the first twenty. During the course of these fifty treatments, several patients began to show organic psychotic symptoms, such as untidiness, impairment of intellectual functions and marked regression, and therapy was interrupted for several weeks until these symptoms subsided. In all treated cases, whenever marked confusion was evidenced treatment was interrupted until the confusion had disappeared. In the technic of treatment, it was the object always to produce a major convulsion, since it was observed that in some cases a subconvulsive seizure delayed improvement.

In the manic-depressive depressed cases, good results were obtained from an average of eight treatments. The involutional melancholia cases required an average of fifteen treatments. The manic-depressive manic cases required an average of twenty treatments. In the acute schizophrenic group with a sudden onset, ten to twelve convulsions sufficed. The chronic schizophrenic cases with an insidious onset were refractory to any number of treatments. We have no experience in the use of combined electro-shock and insulin therapy in the latter group.

All improved cases received a certain amount of psychotherapy and reorientation during and following treatment. In a small number of cases, an attempt was made during treatment to give more intensive psychotherapy, in the hope that this would decrease the number of shock treatments required and at the same time give the patient a deeper insight into his problems. The results did not indicate that this method was practical. As soon as the patient became accessible to psychotherapy he invariably occupied his interview with statements to the effect that he had been sick but

\*Senior physician Foxborough State Hospital

†Assistant superintendent Foxborough State Hospital

was now well, ready to go home and not interested in discussing his problems. In addition, the patient's relatives, as soon as they observed improvement, began to press for early home visits, which interrupted attempts at intensive psychotherapy.

In the majority of improved treated cases, the patient soon began to *object* to further treatment and had a tendency to cover up his remaining symptoms in an effort to convince the physician that treatment should be discontinued. This attitude is not conducive to a frank and open discussion of existing psychogenic problems and conflicts. In view of this, it seems that intensive psychotherapy must of necessity be carried on after the patient's release from the hospital. Although these patients are required to report at the hospital at regular intervals, — approximately once a month for one year, — this is not sufficient for intensive psychotherapy. An exception to this conclusion was encountered in the psychoneurotic group, in which a few electric-shock treatments greatly facilitated psychotherapy.

Although the maximum number of shock treatments has not been definitely established and some clinicians advocate the administration of three or four series of twenty treatments each, one often doubts that this is a sound therapeutic procedure, especially in view of the much more favorable results reported in chronic schizophrenia with insulin-shock therapy.

During the three years in which we have employed electric-shock therapy, approximately 4000 treatments have been administered and complications have been negligible. There have been no fatalities and no fractures of the spine or other bones. Temporary confusion and more prolonged impairment of memory were the most frequently encountered complications. In some cases impairment of memory lasted for three months after cessation of therapy. In the cases that received fifty treatments, some patients showed symptoms pointing to the possibility of organic brain damage.

One patient developed signs of active pulmonary tuberculosis after receiving his fifteenth convulsive shock. Another developed pulmonary tuberculosis three months after receiving fifty treatments. A young, robust male patient developed pleural effusion with high fever during the course of convulsive therapy.

Four patients with the diagnosis of dementia praecox, paranoid type, developed definite assaultive tendencies during the treatment, and 2 of these threatened suicide and made suicidal gestures. Two patients developed grand-mal seizures within two months of cessation of treatment.

#### CLINICAL RESULTS AND DISCUSSION

The difficulties encountered in evaluating the clinical response to this type of therapy are many

and are no doubt the cause of the great discrepancies noted in the results obtained in reports from different hospitals. The greatest disagreements noted are in the reported results in schizophrenia. The cases included under this heading represent a heterogeneous group with a great variation in etiology and prognosis. The results obtained from electro-shock therapy therefore depend greatly on the type of cases selected for treatment.

To evaluate this empirical therapeutic agent, our results must be compared with those obtained in the same hospital before institution of this therapy, and also with those obtained in other hospitals with electroconvulsive treatment.

Kalinowsky<sup>1</sup> and Lowinger and Huddleson<sup>2</sup> have emphasized that the efficacy of electric-shock therapy in schizophrenia depends on the length of illness before treatment is instituted and the intensity with which treatment is given. In acute schizophrenic cases Kalinowsky reported 68 per cent remissions, whereas in chronic cases he reported only 9 per cent. Many clinicians obtained no remissions in cases with a duration of two years or more.

We too have learned that the time element is of great importance in the prognosis to be expected from shock therapy, but we believe that the *mode* of onset, the age of the patient at onset, the severity of symptoms and evidence of marked maladjustment beginning in adolescence are the best criteria for prognosis. We have failed to obtain remissions in several acute cases of schizophrenia regardless of the number of treatments prescribed. In these cases the failure could not be ascribed to the length of illness or the lack of intensive treatment. In certain cases, in spite of repeated courses of this therapy we witnessed the return of a foggy, dreamy, confused state after only a few lucid days.

There are also technical difficulties encountered in reporting statistical results of electric-shock treatment. Acute schizophrenia gave a high percentage of remissions, ranging from 60 to 75 per cent, whereas in patients who had been ill for a year or more before treatment was begun the remissions ranged from 2 to 9 per cent. Any report of results that lumps together these two groups is extremely misleading.

There were also certain patients who after treatment had a full remission that lasted sufficiently long to accomplish their discharge from the hospital but promptly developed another episode, were readmitted as new cases, were treated again and were once more released. Others were subsequently admitted to other hospitals for treatment. In some reports these cases appear several times as recovered cases.

In certain reports it is noted that patients improved but required weekly treatments outside the hospital to maintain this improvement. We have such cases, but it is our opinion that they cannot

be considered as improved and are not properly classified as such

In addition, there is always a group of schizophrenic patients who present many symptoms of an affective psychosis and are often described as having schizo-affective disorders. Most of these cases have a good prognosis with any form of treatment and do not necessarily prove the effectiveness of electro-shock therapy in schizophrenia. One is often tempted to revise this diagnosis in reviewing these cases.

For purposes of simplification, our results are recorded in two groups — that of patients who recovered or were much improved and are living outside the hospital, and that of patients not well enough to leave the hospital (Table 1).

Of the 175 schizophrenic patients treated, 120 had been ill for one year or more and 55 had been ill for less than one year. With the latter the re-

mission rate was 62 per cent, with an average hospitalization period of less than six months, with the former the remission rate was 7 per cent. In patients with manic-depressive psychoses, the remission rate was 70 per cent, with the average hospitalization period seven months. In involutional melancholia, the remission rate was 48 per cent, and in psychoneurosis, 80 per cent. Our results on the whole do not differ greatly from those obtained by Kalinowsky in his report of 1500 cases. He gives his remission rates as follows: manic-depressive psychosis, 85 per cent, acute schizophrenia, 54 per cent, schizophrenia of two years' or more duration, 9 per cent, involutional melancholia, 85 per cent, and involutional paranoia, 43 per cent.

of shock therapy, we have reviewed the records of all patients admitted during 1937 and 1938. During this period there were admitted 100 patients diagnosed as having dementia praecox, 60 per cent of these cases were acute. Two years after admission 24 patients had been discharged, 4 had died, and 72 were in the hospital or had been transferred to other hospitals. Of 33 manic-depressive patients, 17 were out of the hospital, and of 17 patients with involutional psychoses, 5 were out of the hospital. The average length of hospital stay for the schizophrenic patients discharged was sixteen months and that for manic-depressive patients was eleven months.

In the second group, — namely, the patients improved but still hospitalized, — the record is as follows. In the whole group of affective disorders treated, all the patients showed slight improvement in behavior and several have been able to go on short visits. The involutional patients who did not improve sufficiently to leave the hospital improved in physical health and are now employed in various hospital departments.

The great majority of the treated patients with chronic schizophrenia gave a history of insidious onset and showed mutism and bizarreness, with flattening of the emotions. They usually showed some improvement after five or six treatments, but as treatment progressed they tended to regress even further than when treatment was instituted. The paranoid schizophrenic patients became more irritable, stubborn, resistive and assaultive, and treatment was discontinued.

A number of patients who presented marked difficulties in management of several years' duration improved with treatment sufficiently to adjust well on the wards with other patients.

CONCLUSIONS

Three years' experience with electric convulsive therapy has convinced us of its efficacy in the treatment of acute psychoses of functional origin. The length of the psychotic episode was definitely shortened, as is indicated in the figures covering patients admitted in 1937 and 1938 who had no shock treatments, the period of hospitalization was less hazardous, and in acute cases the number of remissions was almost doubled.

As regards the efficacy of this form of treatment in schizophrenia, the results are generally good if treatment is instituted early in the disease and if the cases are of sudden onset and do not show early marked regression.

In the treatment of chronic dementia praecox, we are convinced that electric convulsive therapy is not of much value. We do not feel justified in treating 100 patients with the hope of obtaining seven remissions.

TABLE 1 Summary of Clinical Results

RESULT	NO OF CASES	PERCENTAGE
Recovery or much improvement (outside hospital)		
All patients	123	46
Men	57	52
Women	66	42
Moderate or little improvement (inside hospital)		
All patients	143	54
Men	53	43
Women	90	58

mission rate was 62 per cent, with an average hospitalization period of less than six months, with the former the remission rate was 7 per cent. In patients with manic-depressive psychoses, the remission rate was 70 per cent, with the average hospitalization period seven months. In involutional melancholia, the remission rate was 48 per cent, and in psychoneurosis, 80 per cent. Our results on the whole do not differ greatly from those obtained by Kalinowsky in his report of 1500 cases. He gives his remission rates as follows: manic-depressive psychosis, 85 per cent, acute schizophrenia, 54 per cent, schizophrenia of two years' or more duration, 9 per cent, involutional melancholia, 85 per cent, and involutional paranoia, 43 per cent.

Our comparatively low figure of 46 per cent of treated patients well enough to live outside the hospital is accounted for by the fact that almost half the 266 patients treated had chronic schizophrenia, and also by the fact that many of the involutional melancholia cases were of the paranoid type. Especially good results were obtained in a group of young women who developed schizophrenic symptoms following delivery, and also in a group in whom fatigue appeared to be a precipitating factor.

In order to compare our results with those obtained in the same hospital prior to the institution

Although we have had no personal experience with insulin-shock therapy or combined electric-shock and insulin-shock therapy, we are impressed by the results reported by other hospitals. It is our hope that as soon as hospital conditions permit we shall be able to treat with insulin a group of cases that proved refractory to electroconvulsive therapy.

Electric-shock therapy is of value as symptomatic treatment in chronic hospital cases presenting marked difficulties in management, provided that

symptoms can be alleviated with a few treatments and that maintenance treatment is not required too frequently.

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## MEDICAL PROGRESS

### GYNECOLOGY CARCINOMA OF THE VULVA

LANGDON PARSONS, M.D.,\* AND JOE VINCENT MEIGS, M.D.†

**L**ITTLE progress has been made in the treatment of carcinoma of the vulva during the last five years, except for a more enlightened conception of the natural lymphatic spread of the disease and emphasis on a more radical surgical approach to the deep lymphatic chains.

Among those primarily interested in the disease, the battle for early recognition and preventive treatment has continued. Despite the many articles appearing in the literature, the patient still presents herself to the operating surgeon with a relatively advanced state of malignancy. Through the medium of the radio, which has taken the place of the corner drugstore, home therapy in the form of soothing salves for relief of intolerable itching or pain has often been tried for several months. The medical profession appears to be not entirely blameless, for there are few conditions in the field of malignant disease that are so badly misdiagnosed and maltreated as is carcinoma of the vulva.

The problem therefore revolves around early recognition of the prodromal symptoms on the part of the patient and, similarly, greater alertness on the part of the physician to the early manifestations either of the premalignant state or of the actual presence of the cancerous lesion. The surgeon for his part must adopt a more radical approach to the eradication of the neoplasm, as regards both the initial lesion and its distant spread.

Such a change in attitude on the part of the laity and the medical profession is of the greatest importance, for the disease in its actual course tends

to remain localized for long periods, metastasizing to distant organs slowly, although freely. An attack may therefore be made on the local lesion and the regional lymphatics with a reasonable hope of cure, provided that a radical enough concept is entertained at the time of the initial attack. For the patient to temporize because of a natural reluctance to consult a physician for an itching vulva or for her to prolong self-treatment with ointment, salve or hormones is to underestimate the disease. An inadequate choice of a surgical approach, such as the use of radium or x-ray, partial vulvectomy, hemivulvectomy or complete vulvectomy with a unilateral superficial groin dissection, is to court disaster.

It appears that the dissemination of knowledge regarding the nature of carcinoma of the vulva has been faulty in that neither the public nor the medical profession is aware of the tragic consequences of neglect in a disease that should present one of the highest possibilities of complete cure of any of the cancerous lesions. Undoubtedly this is due in part to the fact that carcinoma of the vulva represents only 4 per cent of the total cases of genital cancer in women. Thus, although any cancer educational program is followed by the appearance in clinics and private offices of many early or suspicious cases of cancer of the cervix or fundus of the uterus, the same cannot be said for cancer of the vulva.

So far as faulty diagnosis on the part of the physician first consulted is concerned, there are several factors at work. One of these is the failure to recognize the true cancerous state, such as the difference between kraurosis and leukoplakia. Likewise, most physicians have been taught that a cancer is, by and large, nontender. For the most part this is true, but the vulva, like the floor of the mouth, is a notable

\*Instructor in surgery, Harvard Medical School; visiting surgeon, Massachusetts General Hospital, surgeon, Pondville Hospital; surgeon, Palmer Memorial Hospital.

†Clinical professor of gynecology, Harvard Medical School; chief of the Vincent Memorial Hospital (Gynecological Service), Massachusetts General Hospital, surgeon, Pondville Hospital; gynecologist, Palmer Memorial Hospital.

exception. The tenderness is probably due to superimposed infection, but the fact that the lesion is tender is enough to divert the attention of the physician from entertaining a suspicion of cancer.

The surgeon dealing with carcinoma of the vulva is likely to be confronted with a patient in the older age group, for the mean average age of these patients lies somewhere between fifty-eight and sixty-one years. The lesion may appear to be unilateral, and the nodes in the superficial groin, if considered at all, may be regarded as inconsequential. The surgeon is thus lulled into a sense of security and either attempts a wide local excision or hemivulvectomy or applies radium locally. If he elects to perform a groin dissection, this is usually undertaken at a later date when it is evident that the nodes previously regarded as insignificant represent metastases. If the dissection is done as part of the original operation or as a staged procedure, it is likely to be a superficial removal of the nodes above Poupart's ligament.

In the first place, cancer of the vulva is a disease of the entire vulva, and the surgeon performing a hemivulvectomy or local removal is more often than not confronted with a contralateral neoplasm or a local recurrence. Neoplasms in this area are prone to recur.

As for the lymphatic spread, there is a marked tendency, depending on the location of the initial lesion, both to bilateral invasion of the regional lymphatics in the groin and to invasion of the deep femoral chain located above Poupart's ligament, where the nodes in the obturator area and Cloquet's node along the external iliac vein are frequently involved. None of these areas can be reached by a superficial node dissection in the groin.

It is thus apparent that many surgeons have fallen into the trap of underestimating their opponent while attempting to spare their patients a more formidable surgical experience. If at the end of six months or one year a local recurrence is observed and the nodes of the groin become obviously involved, the patient must then undergo the same degree of surgery when she is one year older and has less chance of a permanent cure.

#### DIFFERENTIAL DIAGNOSIS

All writers on this subject agree that all tumors of the vulva should be biopsied, whatever the size of the lesion and whatever the age of the patient. Thus, Speisser<sup>1</sup> writes as follows:

A positive diagnosis should never be made solely on the appearance of infected lesions about the external genitals. Grossly similar lesions may result from different etiologic factors or a single agent may produce variable lesions. Since many of the pathognomonic factors may be absent it is well to do routinely a dark-field and serologic examination, smear for Donovan bodies, Ducrey bacillus and fusospirochetes, intradermal test with Ducrey bacillus antigen and the Frei antigen and a microscopic examination after biopsy.

Carcinoma of the vulva is infrequently found in Negroes, but certain writers have found, as Deibert and Greenblatt<sup>2</sup> have, that genital cancer may be coexistent with, be stimulated by, or form a direct sequel to venereal disease, particularly lymphogranuloma. Eight of the 9 cases of carcinoma of the vulva occurring in the Negroes in Taussig's<sup>3</sup> series were preceded by syphilitic or postsyphilitic granulomas.

The reader is referred to the recent excellent articles by Speisser,<sup>1</sup> Taussig<sup>3</sup> and Savill<sup>4</sup> for detailed information on the subject of infectious diseases. Neoplasms in the area of the vulva have been discussed in the recent literature by Norris and Block,<sup>5</sup> Folsome,<sup>6</sup> and MacDonald.<sup>7</sup>

#### PREVENTION

That certain changes in the tissues of the vulva area predispose to malignant transformation is a well known fact. Leukoplakia, for example, is universally regarded as precancerous because of the tendency to epithelial hypertrophy. Thus, Taussig<sup>3</sup> found that 71 (45 per cent) of 161 patients with carcinoma of the vulva had a preceding leukoplakia. During the same period he observed twice this number of cases of leukoplakia without carcinoma. In other words, one third proceeded to the development of carcinoma. One would therefore expect prophylactic vulvectomy to produce a cure and reduce the incidence of subsequent cancer. Kraurosis, on the other hand, is an atrophic process developing in elderly women or in castrates and, as Savill<sup>4</sup> points out, the pre-existing atrophy prevents the development of the hypertrophic state with keratinization seen in leukoplakic vulvitis.

It therefore appears to be a simple process of selection to provide the proper treatment in the prevention of the cancer. Vulvectomy is definitely indicated in leukoplakia, whereas the vulva with kraurosis should readily respond to therapy with estrogens, whether these are applied locally or parenterally, or to vitamin A and dilute hydrochloric acid orally, as suggested by Swift,<sup>8</sup> who believes that lack of vitamin A with varying degrees of achlorhydria underlies the pathologic state found in kraurosis, leukoplakia and pruritus vulvae.

Unfortunately, despite a voluminous amount of literature, dating back to the Hunterian lectures of Bonney in 1909, regarding the difference between kraurosis and leukoplakia, confusion still exists. It seems that the two conditions may exist simultaneously in the same patient. Graves and Smith<sup>10</sup> and Adair and Davis<sup>11</sup> believe that they are one and the same process, whereas Ketron and Ellis<sup>12</sup> think that each may be identified in the early stages, although they may be present together. The problem is thus not quite so simple as it first appears. Excellent descriptive articles bearing on the discussion of the difference between these conditions may be found in the literature. Savill,<sup>4</sup> Buxton,<sup>13</sup>

Taussig,<sup>3</sup> and Norris and Block<sup>5</sup> have been recent contributors

Perhaps one should adopt the attitude of Norris and Block<sup>5</sup> toward prophylactic vulvectomy. These authors write

Physiologic atrophy of the vulva predisposed to pathology. The sequence of events would be the development of minute cracks in this early traumatized atrophic area, followed by infection, itching, more trauma through the years, to the final stage of chronic atrophic dermatitis manifest by a smooth, glistening, translucent parchment-like skin in which the pruritus may be intermittent

In this group vulvectomy is advised

Taussig<sup>3</sup> found the following possible etiologic factors in the development of carcinoma of the vulva among 155 cases: leukoplakia, 72 cases, syphilis or postsyphilitic vulva, 9, senile warts, 8, Bartholin's abscess, 4, urethral caruncle, 3, trauma, 3, and no lesion, 58. He makes the following recommendations, based on the suggested etiologic factors, concerning prevention of the disease: complete vulvectomy for leukoplakia, with a rigid follow-up, intensive antisyphilitic treatment in tertiary lesions of the vulva, especially in Negroes, removal of warts on the vulva in the postmenopausal age, close observation or excision of enlarged Bartholin's glands after the age of forty, and cautery excision or radium treatment of urethral caruncles.

### *Estrin Therapy*

The use of estrogens, particularly for the pruritus frequently accompanying kraurosis, has become widespread. Taussig<sup>3</sup> points out that although estrin therapy may decrease pruritus, a carcinogen may be dangerous on a precancerous leukoplakic base where the underlying pathologic state is one of hypertrophy. It is obvious that in view of the existing confusion on the question whether kraurosis and leukoplakia coexist or are one and the same process, estrin therapy has frequently been used for leukoplakia. Rust,<sup>14</sup> Buxton,<sup>13</sup> Foss,<sup>15</sup> Klasten,<sup>16</sup> and Finkler and Marks<sup>17</sup> report a high percentage of cures, whether the estrogens are applied locally as a salve, rectally in the form of suppositories or parenterally as injections. Savill,<sup>4</sup> however, believes that most cases are relieved and not cured. The success or failure of the treatment is based on relief obtained from pruritus and burning. Savill thinks that kraurosis of itself has no symptoms and that the pruritus is but a manifestation of infection. Symptoms recur when the infectious foci again become active. Thus, estrin may be said to relieve symptoms, but the improvement is transitory, and moreover its use in leukoplakia vulvitis may be regarded as dangerous.

### TREATMENT OTHER THAN RADICAL SURGERY

#### *Radiation*

Radiation therapy, either by application or by local infiltration of radium needles or by generalized

x-ray treatment centered over the vulva, has recently been evaluated. The reports are universally discouraging. Healey<sup>18</sup> at the Memorial Hospital in New York City finds that the normal vulva does not tolerate radiation and that prolonged and extensive ulceration results, with slough, causing widespread necrosis of normal tissue, great suffering and actual shortening of life. When attempts were made to treat the local lesion with radium and the groin with x-rays, the local damage was so severe that the latter was either postponed or omitted. Folsome,<sup>6</sup> who used radiation therapy alone or in combination with surgery in a series of 128 cases, found it to be ineffective. Stoeckel<sup>19</sup> in a compilation of 126 cases found only 12 per cent five-year survivals. Plate<sup>20</sup> in England and Graves and Mezer<sup>21</sup> in this country had no five-year survivors following radiation therapy.

As regards the use of x-ray treatment in distant nodes, Taussig<sup>22</sup> states that a metastatic node is more resistant than is the primary lesion. An irradiated node is an uncertain quantity, for, as Stewart and Farrar<sup>23</sup> observe, there are marked differences in radiation response, not only in adjacent nodes but also in different areas in the same node.

The advantage of radiation therapy is that it carries no primary mortality. This is far outbalanced by the complete ineffectiveness of the treatment, not to mention the profound discomfort associated with its use, whether by radium or by x-ray.

### RADICAL SURGICAL TREATMENT

Despite the fact that there is a marked tendency for carcinoma of the vulva to metastasize freely, in common with all genital cancer, Taussig<sup>24</sup> finds 70 per cent of the cases suitable for the optimum approach to cure—namely, complete vulvectomy with radical bilateral groin dissections. That free metastases do occur is evidenced by the finding of 88 (57 per cent) of 155 cases in Taussig's series and 87 (48 per cent) in the 183 cases of Taylor and Nathanson.<sup>25</sup> This is in part due to long delay by the patient in seeking the physician or by the physician in presenting the patient for proper surgery. The delay in Taussig's series of 155 cases was as follows: less than three months, 7 cases; three to six months, 48 cases; seven to twelve months, 24 cases; thirteen to twenty-four months, 34 cases; over two years, 24 cases; and insufficient data, 18 cases. All writers agree that the worst examples of inexcusable delay, mistaken diagnosis and faulty treatment occur in the treatment of carcinoma of the vulva.

#### *Local Lesion*

When a diagnosis of malignant tumor of the vulva, at any age, whether or not ulcerated, has once been established by biopsy, a wide vulvectomy, including the perianal skin, should be performed either by

sharp-knife dissection or by diathermy. If the skin cannot be closed, it should be allowed to granulate in. The perineal defect may be closed by a posterior vaginal-wall flap.

Although it is true, as noted by MacDonald,<sup>7</sup> that low grade basal-cell lesions, so-called "hydradenoma" (sweat-gland carcinoma) and carcinoma in situ (Bowen's disease)<sup>26, 27</sup> are said to respond to a purely local excision, there appears to be general agreement that there is no place in the treatment of carcinoma of the vulva for a partial vulvectomy or hemivulvectomy. Taylor and Nathanson,<sup>23</sup> among others, have pointed out the marked tendency toward the development of double lesions, local recurrence or new lesions in this area. We have had a case in which Bowen's disease recurred after an extensive incision. The treatment of choice for the local lesion in malignant tumors of the vulva is a wide, complete vulvectomy. The treatment is not without its mortality, for Taussig had 4 deaths in patients over seventy-two years of age among 117 cases.

Radical vulvectomy does not always produce a cure. This is certainly due to the relatively advanced state of the disease when first encountered. Taussig<sup>24</sup> groups his cases in five stages, as follows: Group 1, patients without palpable metastases, and a tumor 1 to 3 cm in diameter; Group 2, patients without palpable metastases, and a tumor 4 to 7 cm in diameter; Group 3, patients with a tumor over 7 cm in diameter or smaller tumors, with evident but movable metastases; Group 4, patients with extension to the vagina or subpubic space or with large, fixed lymph nodes; and Group 5, far-advanced cases with broken-down lymph nodes and cachexia. The percentage distribution of Taussig's and Folsome's<sup>6</sup> cases, according to this classification, is given in Table 1. Taussig's figures

of cures is not forthcoming. Taylor and Nathanson advance the most evident reasons. First, there is a high incidence of local recurrence or recurrence of the primary lesion, too many local excisions and hemivulvectomies are done. Second, although 20 per cent of patients have deep-node involvement, groin dissections in the past have been superficial rather than radical. Third, too few bilateral dissections have been done, although a high percentage of patients have bilateral metastases, especially when the midline is encroached on. Fourth, there is reluctance in the older age group to do radical dissections, with a resultant increase in the number of superficial dissections. Lastly, because of the patient's age or the uncertainty of regional node involvement, groin dissection is postponed until too late.

### Regional Lymph Nodes

The propensity of the primary lesion, for free metastasis, despite its relatively slow development, has already been commented on. Taylor and Nathanson<sup>23</sup> have observed that clinical appraisal is inaccurate in 30 per cent of cases. Thus, only 70 per cent of the nodes regarded as positive are correctly diagnosed. This is largely due to the associated inflammation frequently accompanying lesions of the vulva. The more important observation, however, is that when no nodes are palpable in the groins, radical dissection shows metastatic involvement in 30 per cent. Thus, when in the case of an elderly woman the surgeon pursues a policy of watchful waiting, under the misguided impression that he is following a conservative course of therapy, he is doing so with one strike already called against him, of which he is unaware. No experienced gambler would take this chance. In 55 per cent of cases the nodes are manifest within the first year, whereas in 70 per cent they appear within two years, the average mean time is six months. Twenty-two per cent demonstrate a belated appearance of nodes, but almost invariably this train of events follows a recurrence of the primary lesion. Thus, to postpone groin dissection because of the age of the patient is to increase by one or two years the age at which she must undergo radical surgery and to decrease her chance of cure.

Some indication of the likelihood of cancerous involvement is given by the size of the palpable node in the groin. As previously stated, 30 per cent are positive when no nodes are palpable, and Taussig found that 18 per cent were positive when the nodes were smaller than 1 cm. When the node is greater than 1 cm, 64 per cent are positive.

Likewise, a consideration of the primary lesion may be helpful in determining the likelihood of regional node metastases. In general it may be said that the size of the lesion is the most important single factor. Undoubtedly this bears a relation to the tendency to encroach on the midline, where

TABLE 1 Classification of Cases of Carcinoma of Vulva

GROUP	NO OF CASES		PERCENTAGE	
	TAUSSIG	FOLSOME	TAUSSIG	FOLSOME
1	28	10	18	8
2	48	22	31	17
3	43	40	28	31
4	29	43	18	34
5	7	13	5	10
Totals	155	128		

lead him to conclude, as have Taylor and Nathanson,<sup>23</sup> that the size of the initial lesion is the largest single factor in the prognosis. It is therefore not surprising that Taylor and Nathanson find that 41 per cent of 170 treated cases had a local cure for five years. Levin and Clarke<sup>28</sup> give the same figure. This represents in both series the summary of all forms of surgical attack on the local lesion and not that of radical vulvectomy.

Inasmuch as patients rarely die of remote metastases, the question arises why a higher percentage

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Taussig<sup>3</sup> found the following possible etiologic factors in the development of carcinoma of the vulva among 155 cases: leukoplakia, 72 cases; syphilis or postsyphilitic vulva, 9; senile warts, 8; Bartholin's abscess, 4; urethral caruncle, 3; trauma, 3; and no lesion, 58. He makes the following recommendations, based on the suggested etiologic factors, concerning prevention of the disease: complete vulvectomy for leukoplakia, with a rigid follow-up; intensive antisiphilitic treatment in tertiary lesions of the vulva, especially in Negresses; removal of warts on the vulva in the postmenopausal age; close observation or excision of enlarged Bartholin's glands after the age of forty; and cautery excision or radium treatment of urethral caruncles.

### *Estrin Therapy*

The use of estrogens, particularly for the pruritus frequently accompanying kraurosis, has become widespread. Taussig<sup>3</sup> points out that although estrin therapy may decrease pruritus, a carcinogen may be dangerous on a precancerous leukoplakic base where the underlying pathologic state is one of hypertrophy. It is obvious that in view of the existing confusion on the question whether kraurosis and leukoplakia coexist or are one and the same process, estrin therapy has frequently been used for leukoplakia. Rust,<sup>14</sup> Buxton,<sup>15</sup> Foss,<sup>16</sup> Klasten,<sup>16</sup> and Finkler and Marks<sup>17</sup> report a high percentage of cures, whether the estrogens are applied locally as a salve, rectally in the form of suppositories or parenterally as injections. Savill,<sup>4</sup> however, believes that most cases are relieved and not cured. The success or failure of the treatment is based on relief obtained from pruritus and burning. Savill thinks that kraurosis of itself has no symptoms and that the pruritus is but a manifestation of infection. Symptoms recur when the infectious foci again become active. Thus, estrin may be said to relieve symptoms, but the improvement is transitory, and moreover its use in leukoplakia vulvitis may be regarded as dangerous.

## TREATMENT OTHER THAN RADICAL SURGERY

### *Radiation*

Radiation therapy, either by application or by local infiltration of radium needles or by generalized

x-ray treatment centered over the vulva, has recently been evaluated. The reports are universally discouraging. Healey<sup>18</sup> at the Memorial Hospital in New York City finds that the normal vulva does not tolerate radiation and that prolonged and extensive ulceration results, with slough, causing widespread necrosis of normal tissue, great suffering and actual shortening of life. When attempts were made to treat the local lesion with radium and the groin with x-rays, the local damage was so severe that the latter was either postponed or omitted. Folsome,<sup>6</sup> who used radiation therapy alone or in combination with surgery in a series of 128 cases, found it to be ineffective. Stoeckel<sup>19</sup> in a compilation of 126 cases found only 12 per cent five-year survivals. Plate<sup>20</sup> in England and Graves and Mezer<sup>21</sup> in this country had no five-year survivors following radiation therapy.

As regards the use of x-ray treatment in distant nodes, Taussig<sup>22</sup> states that a metastatic node is more resistant than is the primary lesion. An irradiated node is an uncertain quantity, for, as Stewart and Farrar<sup>23</sup> observe, there are marked differences in radiation response, not only in adjacent nodes but also in different areas in the same node.

The advantage of radiation therapy is that it carries no primary mortality. This is far outbalanced by the complete ineffectiveness of the treatment, not to mention the profound discomfort associated with its use, whether by radium or by x-ray.

## RADICAL SURGICAL TREATMENT

Despite the fact that there is a marked tendency for carcinoma of the vulva to metastasize freely, in common with all genital cancer, Taussig<sup>24</sup> finds 70 per cent of the cases suitable for the optimum approach to cure—namely, complete vulvectomy with radical bilateral groin dissections. That free metastases do occur is evidenced by the finding of 88 (57 per cent) of 155 cases in Taussig's series and 87 (48 per cent) in the 183 cases of Taylor and Nathanson.<sup>25</sup> This is in part due to long delay by the patient in seeking the physician or by the physician in presenting the patient for proper surgery. The delay in Taussig's series of 155 cases was as follows: less than three months, 7 cases; three to six months, 48 cases; seven to twelve months, 24 cases; thirteen to twenty-four months, 34 cases; over two years, 24 cases; and insufficient data, 18 cases. All writers agree that the worst examples of inexcusable delay, mistaken diagnosis and faulty treatment occur in the treatment of carcinoma of the vulva.

### *Local Lesion*

When a diagnosis of malignant tumor of the vulva, at any age, whether or not ulcerated, has once been established by biopsy, a wide vulvectomy, including the perianal skin, should be performed either by



and the dissection is continued laterally. By blunt dissection and retraction the deep epigastric vessels are exposed at the point where they form the medial border of the internal ring. Exposure and ligation of these vessels close to their point of origin is the secret of the entire dissection. It is then possible to reflect the abdominal wall with the round ligament to expose the peritoneum bulging into the iliac fossa. The extent to which the peritoneum may be reflected, giving access to all the retroperitoneal structures in relation to the great vessels, is limited only by the obesity of the patient. The dissection is begun high up. The ureter is found lying medially on the peritoneum. The femoral nerve is identified near the ligament, running laterally to join the femoral vessels. The obturator nerve is found readily in the obturator space laterally.

Starting from above and laterally, the dissection proceeds as the tissue is mobilized medially and downward in relation to the iliac vessels. The obturator nodes are found in the space lying on the obturator internus muscle in association with the obturator nerve. Near the stump of the epigastric vessel nodes are found from the lateral side of the artery to the medial side of the vein, where the external iliac nodes are oftenest involved. The dissection is completed by freeing the tissue medial to the vein in the femoral canal.

The wound is reconstructed, irrigated with saline solution and closed without drainage. The defect in the femoral canal is closed by suturing pectineus fascia to the inguinal ligament. The skin is trimmed to permit a tight closure of the wound without drainage. Pressure dressings are firmly applied, the lower leg is bandaged, and the leg is immobilized for ten days. If at the first dressing serum has collected, it may be aspirated with a syringe and needle. By following this simple procedure the necrosis of the skin edges of the incision observed by Taussig in 90 per cent of his cases has been reduced to a minimum.

264 Beacon Street

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bilateral metastases are most evident. Taylor and Nathanson, for example, discovered only 10 per cent bilateral metastases with a unilateral primary lesion, but 27 per cent when the primary disease included or approached the midline. When the size of the initial growth on the vulva is combined with high malignancy and long duration, regional metastases may be expected. In this regard ulcerating lesions are more prone to extend distantly than are papillary lesions, for the latter are by and large of a lower grade of malignancy.

Taussig also believes that the presence of metastasis is of less importance than the size of the primary lesion. His percentage of cures was 11 per cent less in cases with metastases than in those without metastases, whereas lesions greater than 4 cm in size showed 50 per cent fewer cures than the earlier or smaller growths. He further concludes that if a bilateral radical groin dissection is done, the difference between metastatic and nonmetastatic cases measured in terms of five-year survivals is only 11 per cent.

The nodes chiefly involved are the superficial femoral nodes below Poupart's ligament. The secondary spread is by the deep lymphatic nodes to the deep femoral nodes (Rosenmüller's or Cloquet's nodes) or by the inguinal nodes to the external iliac region. It is the latter group that are not touched in the usual superficial groin dissection. Taussig found that in the cases of his series in which the lymph nodes were actually removed, 66 per cent showed involved nodes when a one-sided or superficial operation was done. In the less advanced cases in which a complete radical groin dissection was performed, 41 per cent had metastatic nodes. It is interesting to consider Taussig's five-year survival rate in the light of the above. In the cases in which unilateral or superficial nodes alone were removed there were five-year survivals in only 28 per cent, as against 58 per cent for the more radical, complete dissection.

Moreover, nodes are also found in the obturator space and along the external iliac. The iliac nodes are frequently involved when the lesion is situated along the clitoris.

Where partial or complete removal of the nodes was done, Taussig found 48 per cent of the nodes involved in 95 cases, Taylor and Nathanson found 50 per cent involved in 33 cases.

Inasmuch as Taussig often chooses to perform radical vulvectomy and bilateral radical groin dissections in one stage, the operation is not without its mortality. Age has a direct bearing, for whereas such operations were performed on 45 women under the age of sixty-five with a 2 per cent mortality, operations of the same type in 23 women over sixty-five yielded a mortality of 18 per cent. Vulvectomy alone has an appreciable mortality in the elderly, and 4 of 22 such patients, all over seventy-two years old, died as a result of this procedure. Pos-

sibly the mortality figure for the complete operation can be further reduced if staged procedures are performed.

*Operative technic.* Taussig's modification of the original Basset operation has been adequately described in the literature. Johnston<sup>29</sup> has recently published a further modification for use in the elderly group.

Recently at the Massachusetts General Hospital and at the Pondville Hospital a simple technic for the exposure of the nodes above Poupart's ligament has been routinely employed. This has been described by Taylor and Nathanson<sup>25</sup> but has not otherwise been reported. The groin dissection is followed by an attack on the nodes both below and above Poupart's ligament. The advantage of this procedure lies in the excellent exposure and wide vision obtained as high along the iliac veins or as deep in the pelvis as one cares to go. Excellent direct vision of the obturator space is also obtained. All these are secured by the Bassett procedure described in the textbooks, but the repair of the inguinal ligament after section is formidable. The following procedure accomplishes the exposure without division of the inguinal ligament.

Spinal or gas, oxygen and ether anesthesia is given, depending on the age and general condition of the patient. Local anesthesia is rarely used.

The patient is placed with the leg externally rotated and the feet elevated. A straight incision, with the edges beveled outward, is made over the course of the femoral artery across the inguinal crease and carried halfway to the umbilicus, curving toward the anterior spine if one so desires. The extent of the exposure depends in part on the obesity of the patient but more on the extent of the lateral incision through the external oblique fascia — hence the lateral curve.

The dissection is carried out with a sharp knife down to the muscles beyond the saphenous triangle. The saphenous vein is ligated at the lower angle. The fat, nodes and areola tissue along the great vessels are dissected centrally, the large vessels are identified, and the contributing branches are ligated up as high as the point at which the saphenous enters the femoral vein. The femoral canal is dissected clean, including the areola tissue that fills it. By going above Poupart's ligament and removing the fat and nodes overlying the external oblique muscle a bloc dissection of the entire superficial system is accomplished. The skin of the lower portion of the wound is closed without drainage after thorough irrigation. This marks the end of the superficial portion of the dissection and follows the standard procedure.

In the radical portion of the dissection, the external oblique fascia is incised over the course of the inguinal canal as in a herniotomy, and the round ligament is lifted from its bed, exposing the conjoined tendon. This is divided to the internal ring.

where he was finally regulated at 40 units of protamine zinc insulin and 15 units of regular insulin daily and a high-carbohydrate, low-sodium diet.

**Second admission** (one month later) The patient did well until seven days before entry, when he developed a sore throat and increasing weakness. He also had a dizzy sensation when he bent over. Five days before entry he noticed increasing anorexia and a sharp, constant pain in the right upper quadrant of the abdomen. He had not been drinking much fluid during that time, and his urinary output gradually decreased. The urine also became quite dark in color and gave positive tests for sugar and albumin. He had no dyspnea or orthopnea.

On examination the patient showed a great increase in the slate-gray pigmentation of his skin, with a cyanotic hue, especially marked over the upper chest, arms and face. His face, which had been thin and drawn on the previous admission, was puffy and swollen. The veins of the neck and right arm were strikingly distended. The scleras were muddy. The throat was slightly injected. The chest showed signs of bilateral pleural effusion, and occasional crackling rales were heard at the bases. The heart signs had not changed since the first admission. The abdomen showed marked ascites making palpation difficult, but the liver edge was felt 10 cm. below the costal margin in the mid-clavicular line. There was slight ankle edema. The patient was able to lie quite flat in bed without dyspnea.

The temperature and respirations were normal. The pulse was 94. The blood pressure was 130 systolic, 80 diastolic.

Examination of the blood revealed a red-cell count of 4,000,000, with 11 gm. of hemoglobin. The white-cell count was 15,000, with 66 per cent neutrophils and 30 per cent lymphocytes. The blood sugar was 126 mg. per 100 cc., rising to 364 mg. the next day. At that time the nonprotein nitrogen was 62 mg. per 100 cc. and the carbon dioxide 22.5 milliequiv. per liter. The total protein was 7.0 gm. per 100 cc. with an albumin-globulin ratio of 1.03. The urine showed a green test for sugar and a trace of albumin, but no acetone. The specific gravity was 1.020. The venous pressure in the right arm was equivalent to 340 mm. of water.

An x-ray examination of the chest revealed that since the last examination the diaphragms had become elevated, and this may have accounted for the increase in the size of the cardiac shadow. The cardiothoracic ratio was now 17.5:28.0. The superior mediastinum was somewhat wide. The right leaf of the diaphragm was obscured by irregular areas of increased density in the lung fields, which were probably platelike areas of atelectasis. There was a little fluid in the right pleural sinus.

On the second hospital day, the patient showed pitting edema of the legs up to the knees. Despite penicillin and x-ray therapy to the upper medias-

tinum at the rate of 200r per day for four days, he continued to go downhill rapidly and gradually lapsed into stupor.

An electrocardiogram on the fourth hospital day showed a normal rhythm at a rate of 75, with right-axis deviation. The PR interval was 0.17 to 0.18 second.  $S_1$  and  $S_2$  were prominent.  $T_1$  was upright.  $T_2$  was low upright, and  $T_3$  slightly inverted.  $CF_2$  and  $CF_4$  showed a small R and inverted T. S was prominent in  $CF_4$ . There was a tendency to low amplitude in all leads.

The patient died on the fifth hospital day.

## DIFFERENTIAL DIAGNOSIS

**DR. WALTER BAUER:** The lesion on the nose was evidently a tertiary lesion of syphilis, which disappeared following the administration of potassium iodide.

"He drank a large amount of water and had a urinary frequency of twelve times a day." This is the first suggestion that the patient had hyperglycemia and glycosuria.

Did anyone ever feel the spleen in this patient?

**DR. TRACY B. MALLORY:** It is not recorded.

**DR. BAUER:** Despite his difficulty in walking, unsteadiness and not knowing where his feet were, the Romberg and Babinski signs were negative. Is anything said about his eyes? Did he have Argyll-Robertson pupils or any other neurologic abnormality?

**DR. JOHN B. STANBURY:** All neurologic findings were normal.

**DR. BAUER:** Is the value of 126 mg. in the insulin-tolerance test higher than one would expect, or is it within normal limits?

**DR. STANBURY:** It shows insulin sensitivity.

**DR. BAUER:** But not insulin resistance.

**DR. STANBURY:** That is correct.

**DR. BAUER:** It is obvious that in studying this patient an attempt was made to rule out Addison's disease, as well as to gain evidence that hepatic impairment was present. The accumulated information indicates that he had hyperglycemia, glycosuria and hepatic impairment.

The heart was 13.7 cm. to the left. Did he have fairly marked ascites?

**DR. STANBURY:** Yes.

**DR. BAUER:** So that the cardiac enlargement was thought to be due to displacement?

**DR. STANBURY:** We thought that he had cardiac enlargement.

**DR. BAUER:** I am told that the first electrocardiographic findings are consistent with coronary disease and pericarditis but might be found in other conditions. Evidently they did not persist, as shown by the next electrocardiogram.

Was the diabetes reasonably well controlled?

**DR. STANBURY:** Quite well controlled without difficulty.

# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

EDITH E. PARRIS, *Assistant Editor*

### CASE 32261

#### PRESENTATION OF CASE

*First admission* A forty-six-year-old Lithuanian-American machinist entered the hospital because of fatigue, weakness and abdominal pains not related to meals.

At the age of twenty-two years the patient had a penile lesion and discharge, which were cleared up by his physician. He had no rash and was well until eight years before entry, when an ulcerating, crusted, thickening of the skin appeared on the side of his nose. This lesion brought him to the Skin Out Patient Department, where blood Hinton and Wassermann tests were positive and the spinal-fluid findings were negative. The lesion regressed under potassium iodide therapy. Six years before entry he received bismuth injections for four months. He then lapsed in his treatments, and was not seen until three years before entry, when he was sent in by the Selective Service Board because of a positive serologic reaction. He then received a total of eight arsenic and thirty-seven bismuth injections, when treatment was stopped because of jaundice. At that time he also complained of weakness, nervousness, exertional dyspnea and epigastric pain. Physical examination revealed a blood pressure of 140 systolic, 110 diastolic, tremor of the tongue and fingers, an aortic systolic murmur and slight midepigastric tenderness. The liver edge was 2 cm. below the costal margin. He was placed on a high-carbohydrate diet and felt improved. During the year before entry he received 10 more bismuth injections. Five months before entry he again noticed increasing weakness, fatigue and occasional pains in the lower abdomen, particularly before bowel movements. He also complained of unsteadiness in the dark and a sensation of not knowing where his feet were. He lost about 8 pounds during this period, despite increased appetite.

The patient admitted drinking two or three quarts of ale a day and whisky occasionally. On one occasion he was seen in the Out Patient Department during an attack of delirium tremens. He drank a large amount of water and had a urinary frequency of twelve times a day.

On examination, the patient appeared chronically ill and showed evidence of recent weight loss. There was a questionable faint slate-gray pigmentation of the skin over the entire body. The heart border was percussed 13.7 cm. to the left of the midclavicular line, with the point of maximum impulse in the fourth interspace. A Grade I systolic murmur was heard at the apex and in the aortic area. The lungs were clear. The abdomen was distended, and a fluid wave obtainable. The liver edge was palpable 7 cm. below the xiphoid process and 3 cm. below the costal margin, the liver was hard and slightly tender. There was also tenderness in the right lower quadrant. There was a general hyporeflexia. Romberg and Babinski tests were negative.

The temperature, pulse and respirations were normal. The blood pressure was 128 systolic, 80 diastolic.

The urine showed a brick-red test for sugar and a +++ test for acetone. A potassium ferrocyanide test for hemosiderin was negative.

Examination of the blood revealed a red-cell count of 3,700,000, with a hemoglobin of 11.9 gm., and a white-cell count of 5900, with a normal differential. The fasting blood sugar was 288 mg. per 100 cc. The carbon dioxide was 28 milliequiv. and the chloride 90 milliequiv. per liter. The sodium was 137.0 milliequiv. per liter. The nonprotein nitrogen was 20 mg., the phosphorus 3.0 mg., the alkaline phosphatase 3.2 units, and the total protein 6.15 gm. per 100 cc., with an albumin-globulin ratio of 1:1. The insulin-tolerance test, starting at 206 mg. glucose per 100 cc., showed reduction to 126 mg. in two hours. A Wilder test for adrenal insufficiency\* was negative. The van den Bergh reaction was 0.8 mg. direct and 1.2 mg. total. The cephalin-flocculation test was +++ in forty-eight hours. The bromsulfalein test showed 22 per cent retention. The blood Hinton test was positive. The 17-ketosteroid excretion was 1.8 mg. in twenty-four hours. The spinal-fluid Hinton reaction was positive, but Pandy and gold-sol tests and the cell count were normal. The stool was guaiac positive in two out of four specimens taken. A potassium ferrocyanide skin test and biopsy of the skin were negative for hemosiderin.

X-ray examination of the chest revealed areas of increased density at both bases. The heart was not remarkable. A gastrointestinal series was negative. A cardiogram showed a normal rhythm at a rate of 100, with left-axis deviation. The PR interval was 0.13 to 0.14 second. T<sub>1</sub> and T<sub>2</sub> were flat, and T<sub>3</sub> slightly inverted. TCF<sub>2</sub> and TCF<sub>4</sub> were inverted, and TCF<sub>3</sub> was diphasic.

The patient improved somewhat on a diabetic regime. On the tenth hospital day he developed slight ankle edema, which persisted. He was discharged after twenty days to the Diabetic Clinic.

\*Cutler, H. H., Power, M. H., and Wilder, R. M.: Concentrations of chloride, sodium and potassium in urine and blood: their diagnostic significance in adrenal insufficiency. *J. A. M. A.* 111:117-122, 1938.

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**DR. STANBURY** Quite well controlled without difficulty.

DR. BAUER Can you describe the slate-colored pigmentation in more detail?

DR. STANBURY The striking feature in this patient was the pigmentation. When he first came in he had a faint slate-gray pigmentation, most marked in the thorax and the face. There was some argument about it. At the second admission, two months later, we thought that the pigmentation had increased, extending over the lower part of the body. In addition the upper extremities and face had almost black cyanosis. It was a very striking picture.

DR. BAUER And "slate gray" is the best description you can give?

DR. STANBURY Yes.

DR. BAUER This man has evidence of obstruction of the superior vena cava, probably in the region of the right innominate artery, without associated symptoms. The physician in charge must have thought the patient had some type of infection because penicillin was administered, the temperature was normal, however.

The white-cell count was not unlike that seen in many patients with cirrhosis of the liver, 5000, yet it later rose to 15,000.

The superior mediastinum was somewhat wide. I should like first to see the x-ray films of his chest.

DR. JAMES R. LINGLEY I cannot add anything to the record. This film shows a high diaphragm, which caused the apex to be pushed out slightly, but I doubt that the heart was enlarged at that time. There are bands of density at both bases, perhaps due to partial atelectasis of the lower lobe. This film two months later shows what I think is an actual increase in the size of the heart, despite the high position of the diaphragm.

DR. BAUER Is it consistent with atelectasis?

DR. LINGLEY More so than with effusion, because the outline is preserved. There are increased density, atelectasis at both bases and fluid in the right costophrenic angle.

DR. BAUER What can you say about the mediastinum?

DR. LINGLEY I think that it is probably wide because of the position of the diaphragm, the great vessels being spread out over a greater area.

DR. BAUER I thought it fair to assume that this man had contracted syphilis at the age of twenty-two, and that antisyphilitic treatment was not given until the appearance of a tertiary lesion. It also seems fair to conclude that he had never been adequately treated. It is rather difficult to avoid diagnosing central-nervous-system syphilis, probably tabes dorsalis, on the basis of the symptoms and the positive Hinton test on the spinal fluid. I suppose that the latter was relatively inactive or a burned-out process.

In addition this man exhibited obvious hepatic enlargement and ascites. Hepatic impairment was present as demonstrated by all the tests employed. There were also hyperglycemia and glycosuria. I

prefer to explain these findings on the basis of hemochromatosis, despite the negative skin biopsies. One might rightly argue that this man had been exposed to any number of agents that could have injured his liver. He developed jaundice while receiving arsenic. Whether this was an arsenical hepatitis or a coincidental infectious hepatitis, one cannot determine. If it was infectious hepatitis, could it possibly have been syringe transmitted? He also gave a history of excessive alcoholic intake, which is commonly found in people with cirrhosis of the liver, and last, but not least, he had syphilis, which can also cause liver disease. The description of the liver is not that of gumma of the liver. I prefer to try to tie things together in the manner already stated, namely, that the hepatic disease, the glycosuria and the hyperglycemia were part and parcel of hemochromatosis. Between the first and second admissions he developed what I should interpret to be obstruction of the superior vena cava, probably at the junction of the right innominate vein because the findings were more marked on the right than on the left. This, as I said before, came on without any symptoms, so I think that it is reasonable to assume that he did not have a mediastinal tumor. He probably had an idiopathic thrombosis of the superior vena cava, which, though rare, can occur. If one entertains that diagnostic possibility one might ask whether this man had an ascending thrombosis of the vena cava, which first became evident when impaired venous return from the head, neck and right arm was noted. I should think that that was rather unlikely in view of the fact that the physical examination does not suggest findings of the type we expect to encounter in a man with a gradually ascending thrombus of the venous cava.

There is one finding that I have not explained, namely, the cardiac enlargement. He never exhibited the signs of aortic regurgitation. There have been a few cases of myocarditis reported as being due to hemochromatosis, and such an explanation might apply in this case. I am well aware, however, that it is exceedingly rare. In concluding I shall say that we are dealing with a man who had syphilis, which was never treated properly. He probably had central-nervous-system syphilis, which was quiescent or burned out. In addition, he had hemochromatosis and obstruction of the superior vena cava, the exact cause of the latter I do not know, but I do not believe that it was due to a mediastinal tumor. I assume that this man went into coma of the type that is seen in hepatic insufficiency, although the record is not too clear on this point.

I should gladly receive suggestions or comments. Dr. Richardson, do you want to help me?

DR. WYMAN RICHARDSON I am keeping quiet.

DR. BAUER I have often told Dr. Mallory that these conferences would test our diagnostic acumen more accurately if he handed one of us the record.

and asked us to discuss it, instead of giving it to us several days in advance. I am glad this system was not in effect today. Although I have read this case abstract four times, I am not absolutely certain of my interpretation. For instance, I failed to mention the symptoms referable to the bowel and the finding of the two positive guaiac tests. One might argue that we had overlooked a malignant lesion of the bowel that finally metastasized to the mediastinum. This is possible, the clinical picture, however, is complicated enough, and I prefer to limit my discussion to the above possibilities.

**A PHYSICIAN:** What about the possibility of pericardial effusion to account for the cardiac enlargement?

**DR. BAUER:** I gather that the margins were too distinct for a pericardial effusion. The x-ray picture is more like cardiac enlargement due to myocarditis.

**DR. CHESTER M. JONES:** With chronic hepatic disease and hepatic insufficiency, do you not believe that abdominal pain and leukocytosis are not infrequent at that stage of the game? The white-cell count of 15,000 is not unusual. As a matter of fact I have often seen leukocytosis in certain phases of liver disease.

**DR. ISAAC M. TAYLOR:** What about beriberi?

**DR. BAUER:** I am sure that the terminal cardiac enlargement is consistent with beriberi. I prefer to tie things together in this case, however. I might include other conditions, such as syphilitic myocarditis and syphilitic liver disease, but I think that is making it much too difficult.

**DR. J. H. MEANS:** Are you interested in the body hair?

**DR. BAUER:** Yes, I should like to know about it. I should also like to know about the prostate. I assume that Dr. Mallory will tell us about these, as well as other things.

I am still disturbed that the pigmentation is spoken of as slate colored and not brownish, but I do not believe that one negative biopsy should scare us out. It may or may not have been done properly. Hemochromatosis is not always demonstrated in the skin, it can be confined to viscera.

**DR. MEANS:** How about argyria?

**DR. BAUER:** It sounds more like argyria. That brings another red herring across the path.

**DR. BENJAMIN CASTLEMAN:** Dr. Joseph C. Aub saw the patient and brought out the idea that if he had cirrhosis on a pigmentation basis perhaps he had developed a hepatoma. Hepatoma is quite prone to extend into and to block the vena cava.

**DR. BAUER:** That is a good point. I thought of hepatoma last night but not this morning.

**DR. JONES:** This would be an ideal case for an inspiration biopsy of the liver.

**DR. MALLORY:** One was done.

**DR. BAUER:** I am glad that I did not know about it.

**DR. MALLORY:** We thought that we should let Dr. Bauer have the pleasure of discussing the case without knowing the answer.

As a matter of fact, when the iron reaction was performed on the biopsy specimen the liver cells and also those of the bile-duct epithelium showed blue granules, a characteristic picture of hemochromatosis.

## CLINICAL DIAGNOSIS

Hemochromatosis

## DR. BAUER'S DIAGNOSES

Hemochromatosis

Obstruction of superior vena cava

Tertiary syphilis

Central-nervous-system syphilis, probably tabes dorsalis

## ANATOMICAL DIAGNOSES

Hemochromatosis, generalized, including liver, pancreas, lymph nodes, thyroid and pituitary glands and heart

Cardiac hypertrophy with marked dilatation

Mural thrombus of right auricle

Ascites

Splenomegaly

Hydrothorax

Esophageal varices

Thrombosis of right cephalic vein

## PATHOLOGICAL DISCUSSION

**DR. MALLORY:** At autopsy we found a considerably enlarged liver, weighing 2380 gm. It was dark chocolate brown. The lymph nodes in the hilus were equally dark brown, as were the pancreas and heart.

All of them were full of hemosiderin. Microscopically it was evident that the thyroid, adrenal and pituitary glands were involved. It is rather characteristic of hemochromatosis that pigment deposits are quite marked in most of the endocrine organs. The heart was dilated and extremely flabby, but showed no microscopic abnormality other than moderately severe iron deposits. At autopsy we did not find a thrombosis of the superior vena cava or any of its large tributaries. The right cephalic vein contained a recent jelly-like, dark-red clot, which was not attached to the intima and which extended distally from its termination in the axillary vein for about 5 cm. That seems to explain the distention of the veins in the right arm but not those in the head and neck. There was a thrombus in the right auricular appendage, but I doubt that it was large enough to have caused obstruction at the orifice of the vena cava. Consequently we are left without an explanation for the apparent upper mediastinal syndrome.

**DR. JONES:** Occasionally in any case of cirrhosis, particularly with a great deal of fluid, and if the patient is horizontal and the head not elevated, the

face is puffy and there is marked edema, which disappears when the patient is elevated for twelve hours. This patient also had ascites and peripheral edema.

## CASE 32262

### PRESENTATION OF CASE

A sixty-year-old nurse entered the hospital because of abdominal pain and jaundice.

Ten months before admission the patient experienced an episode of moderate right-upper-quadrant pain and jaundice lasting several days. The icterus quickly faded, but the patient never felt so actively interested in her work or environment after the episode as she had before it and often had intermittent pain and indigestion. During the next ten months she lost about 65 pounds. Three weeks before admission there was a gradual onset of pain in the right upper quadrant of the abdomen and the lower anterior portion of the right chest, associated with severe nausea and vomiting. The pain was aggravated by coughing and respiration. She was seen by a physician, who told her she had gall-bladder disease. A week before admission her appetite failed. On the morning of entry her sister called attention to the yellow color of the scleras. The stools had been yellowish during this illness.

The patient had had diabetes for five years, during which she was on a diabetic diet and took 20 units of protamine insulin daily. She had had a blood pressure of 195 systolic, 90 diastolic for several years, with at least one episode of auricular fibrillation.

On physical examination there was evidence of considerable weight loss. The skin was yellow and dry. There were rales at the bases of both lungs. The diaphragm was high and its excursions diminished on both sides. There was a Grade II apical systolic murmur. The abdomen was distended and tender, particularly in the upper quadrants. A very tender mass filled the right upper quadrant, extending to below the umbilicus. There was also a mass in the left upper quadrant. Peristalsis was diminished. The uterus felt hard and enlarged. No other pelvic mass was palpable.

The temperature was 102.2°F, the pulse 120, and the respirations 27. The blood pressure was 130 systolic, 85 diastolic.

There were 12.5 gm of hemoglobin, and the white-cell count was 6340. The urine had a specific gravity of 1.015. The protein content was + and the sugar reaction green. A foam test revealed bile. The bilirubin was 1.3 mg per 100 cc direct, 1.4 mg indirect. The serum amylase on two successive days was 7 units per 100 cc. The fasting blood sugar was 334 mg per 100 cc, the carbon dioxide content 32.2 milliequiv per liter, the nonprotein nitrogen 41 mg and the serum protein 7.8 gm per 100 cc and the chloride 94 milliequiv per liter. The prothrombin time was 43 seconds (normal, 19 seconds).

The chest film was normal, but a flat film of the abdomen showed several moderately distended loops of small bowel. There were unidentifiable collections of gas high in the right upper quadrant and midabdomen, and a mass seemed to be pressing on the lesser curve of the stomach. The liver was large and apparently continuous with the mass compressing the stomach. There was a tendency toward left-axis deviation in the electrocardiogram. The PR interval was 0.13 second. ST<sub>1</sub> was depressed, ST<sub>2</sub> inverted, T<sub>1</sub> diphasic, T<sub>2</sub> slightly inverted, TCF<sub>1</sub> upright, TCF<sub>2</sub> low upright, and TCF<sub>3</sub> slightly inverted.

In the hospital the temperature fell to 98.6°F within twenty-four hours and remained normal or subnormal thereafter. Abdominal distention and tenderness persisted. Peristalsis was seldom audible. A peritoneoscopy was performed on the seventh hospital day. Widespread adhesions fixed the small bowel so that it did not move out of the pelvis in the extreme Trendelenburg position. The right lobe of the liver and the gall bladder were covered by an apparently inflammatory mass including the colon and the small bowel. In the left upper quadrant on the anterior peritoneal surface there were several 2-mm and larger yellow nodules thought to resemble fibrin. The visualized portion of the left lobe of the liver was normal. There were no metastatic implants anywhere. On the day after the operation there was an episode of sudden sharp pain in the right side of the chest. There were dullness and diminished breath sounds at the right lung base. The pulse and respiration rose moderately, and the skin was sweating and cyanotic. Both calves were tender. In the x-ray examination the right leaf of the diaphragm was elevated. The diaphragmatic shadow could not be made out. The right pleural sinus contained fluid, and there was some reaction in the lung above. In addition there was an air-containing cavity just below the right leaf of the diaphragm, apparently above the liver, with a fluid level 5 cm in length. The serum bilirubin had risen to 1.9 mg per 100 cc direct, 3.1 mg indirect. The fasting blood sugar and prothrombin time had returned to 101 mg per 100 cc and 23 seconds respectively. The chest pain disappeared on the tenth hospital day. On the twelfth hospital day the patient had sudden dyspnea and collapse without pain. The skin was clammy and cyanotic, and the pulse and blood pressure were not obtainable. The percussion note was markedly impaired, and breath sounds depressed over the entire right lower lobe. Loud rhonchi were heard throughout the rest of the lung fields. The neck veins were moderately engorged. The patient died that evening.

### DIFFERENTIAL DIAGNOSIS

DR ARTHUR W ALLEN Before Dr Lingley shows us the x-ray films, I should like to be told the number of hours the patient lived after her second episode.



AN INTERVIEW About four hours

DR. JAMES R. LINGLEY These are the first chest films, showing normal lung fields on both sides and only slight elevation of the right diaphragm and no gas beneath it. The plain film of the abdomen, taken at the same time, shows above the dilated loops of the small bowel, gas in the stomach with a pressure defect on the lesser curvature, which I presume is due to the mass referred to. In addition to the gas in the small bowel and stomach there is a gas-filled cavity beneath the lower border of the liver. That collection of gas is definitely outside the duodenum, and I think that it is too high for the hepatic flexure of the colon. These are the later films of the chest taken eight days after the first examination. They show a marked change. The diaphragm on the right is now elevated, and there is this large air-containing cavity immediately beneath the diaphragm. There is probably some collapse of the lower lobe and a little fluid in the costophrenic angle. The same thing is seen in the lateral view. Here is the film taken of the patient lying on her left side and showing a shift of the fluid level to the left flank. In going over these films I thought also that there was some air in the soft tissues of the abdominal wall on each side. That air is outside the abdominal cavity.

DR. ALLEN We have no film of the chest after her second episode, on the day of death?

DR. LINGLEY No.

DR. ALLEN Are you able to see the hard mass in the pelvis in the first film?

DR. LINGLEY There are some areas in the pelvis that suggest calcification in a fibroid.

DR. ALLEN I suppose that this case is being presented not so much for a differential diagnosis of the primary disease as for a discussion of the events regarding the sudden episodes of discomfort and final death. Without any question, the history is consistent with gallstones, and the physician who made that diagnosis was probably right. The weight loss of 65 pounds from the time of the first episode of pain and admission to the hospital is interesting but may be based entirely on dietary restrictions, perhaps self-imposed because of indigestion and pain with a normal diet.

The three weeks' duration of the illness that brought the patient to the hospital is consistent with the period that an inflammatory process in the gall bladder takes to erode the hollow viscus and sometimes to produce a fistulous tract that may allow a gallstone to be discharged into the gastrointestinal tract and to produce gallstone ileus. Associated with that degree of inflammatory reaction is a pericholecystic inflammatory process, which might involve hepatic flexure and some of the small intestines, as the peritoneoscopist observed.

The probable reason that peritoneoscopy rather than exploration was decided on was the fact that

the patient was in a fairly serious condition, the diagnosis was not well established and she had had the acute inflammatory process for three weeks at the time of entry. We have here a finding by the peritoneoscopist of some interesting yellow nodules scattered about, particularly in the left upper quadrant. He thought that these nodules resembled fibrin, and that might be what they were. One wonders whether these may have represented fat necrosis, which is associated with pancreatitis. The serum amylase, which was normal on two successive days at entry three weeks after the onset of an episode of this sort, is consistent with pancreatitis, and in some of the necrotic types of pancreatitis there is a normal serum amylase, so that pancreatitis cannot be ruled out on the basis of these normal determinations.

It is amazing that the diabetes responded so well, in spite of the patient's precarious condition, and that the fasting blood sugar returned to normal so promptly. This is also a good illustration of how rapidly vitamin K can reduce a high prothrombin level to a comparatively normal reading. The mass that was felt was probably more or less over the right upper quadrant. This red herring of a mass that projects into the lesser curvature of the stomach bothers me somewhat but might be consistent with a pancreatic collection in the lesser peritoneal sac, which is not an unusual association of pancreatitis. The air outside the gastrointestinal tract is consistent with a perforation between the gall bladder and the intestinal tract and fits quite well into the picture of an acute or subacute cholecystitis that had produced perforation with a secondary peritonitis. The air seen in the abdomen following the peritoneoscopy is not very impressive, since during peritoneoscopy a great deal of air is pumped into the peritoneal cavity to separate the viscera from the abdominal wall, this does not mean that there was a free perforation into the peritoneal cavity.

The episode of sudden pain and dyspnea on the day after the peritoneoscopy is consistent with an embolic phenomenon. This woman had been ill and in bed for four weeks by the time peritoneoscopy was performed and this so-called "operative procedure" was not necessarily to blame for the embolus. It is quite likely that there was a thrombosis of the leg veins, which was not taken too seriously because the patient had so many other things the matter with her. The record does not state that following this first episode anything was done to interrupt the superficial femoral veins to prevent further emboli. I suppose the fact that it was not recorded means that this was not done. There are no clear signs of infarct that I can make out in these films, because the area that is probably involved, that is, the right lower lobe, is obscured by the high diaphragm and the surrounding reaction in the lung. I do not suppose that Dr. Lingley would be willing

to say that this is typical of infarct from the roentgenologic point of view

DR LINGLEY It looks like collapse, and that degree of collapse is consistent with an infarct

DR ALLEN So often following these episodes of infarction, the roentgenologist is the man who can say without any equivocation that the lesion is an infarct. Of course the common source of emboli is the deep veins of the leg. We have interrupted the veins on approximately 1300 patients in this hospital to prevent emboli and have markedly decreased the number of patients who have had prolonged convalescences. If left alone these early bland thromboses progress to phlegmasia alba dolens in a high percentage of cases in this community. If the vein is opened, the clots aspirated and the veins interrupted, the convalescence is greatly shortened. The patient may have inflammatory processes in the veins afterward, but these are never so severe as when they are not operated on. Also, the hazard is eliminated in nearly all cases of fatal emboli. We do have a small percentage of patients that have infarcts after this procedure, and those are best treated by the anticoagulant drugs and not by further surgery.

In this case, there is a description of an episode that occurred on the twelfth hospital day, five days after peritoneoscopy and four days after the first episode of pain in the chest. This is a fairly good description of another embolism. There are certain facts about it. The fact that she lived four hours after the episode is somewhat unusual, although possible. One would have to seek for some other explanation for sudden dyspnea and collapse, even without pain. With a drop in blood pressure vasomotor collapse does occur rather suddenly and is associated with other conditions, such as peritonitis, ileus, high intestinal obstruction and perforation of the viscus, but as a rule none of these are associated with sudden dyspnea. I do not know whether the sudden dyspnea can be explained on the basis of the heart disease, but my belief is that she had a second embolus, which was probably the final cause of death.

This was a patient with gallstones, diabetes, subacute cholecystitis, perforation of the gall bladder with pericholecystic abscess, localized peritonitis (not too localized, I might add) and pancreatitis. The probabilities of subdiaphragmatic abscess are great, not on the basis of this fluid level but on the basis that fluid would have been present above the liver and beneath the diaphragm with any such inflammatory process in this region, since fluid goes there with any opportunity, probably brought about by the forces of respiration. The patient was found to have some biliary cirrhosis, which was due to the jaundice. Obviously she had heart disease, and finally she had pulmonary emboli.

DR TRACY B. MALLORY This is a very long and complicated story. Are there any other suggestions?

I wonder if any of the surgical house officers can tell us what was thought on the wards.

DR T. H. GREEN, JR. We thought, as Dr. Allen did, that the patient probably had gall-bladder disease and gallstones, that the gall bladder perforated three weeks before entry and that she developed a subdiaphragmatic abscess that eventually penetrated through into the peritoneal cavity. At the last episode there was some question whether it might have been primary heart failure rather than a pulmonary embolus.

DR MALLORY Dr. Stanbury, have you any comment?

DR JOHN STANBURY I saw the patient briefly one night, following her last episode and I thought that she had a pulmonary infarct. I was unaware of what was going on in the abdomen.

#### CLINICAL DIAGNOSES

Jaundice  
Cholecystitis, with cholelithiasis  
Perforation of gall bladder  
Peritonitis  
Subdiaphragmatic abscess  
Pulmonary infarcts  
Diabetes mellitus

#### DR ALLEN'S DIAGNOSES

Diabetes  
Subacute cholecystitis, with perforation and pericholecystic abscess  
Cholelithiasis  
Pancreatitis  
Subdiaphragmatic abscess?  
Pulmonary embolism  
Biliary cirrhosis  
Jaundice

#### ANATOMICAL DIAGNOSES

Actinomycotic abscesses of peritoneum and liver, with perforation of right diaphragm  
Cholelithiasis and choledocholithiasis  
Chronic cholecystitis  
Double renal pelvis and ureters  
Adrenal hyperplasia, unilateral  
Neurofibromas of stomach  
Leiomyomas of uterus  
Diverticulosis of sigmoid  
Healed pulmonary tuberculosis, apical.

#### PATHOLOGICAL DISCUSSION

DR MALLORY Dr. Allen made about 10 clinical diagnoses, we wound up with a list of 20 anatomical diagnoses. The underlying and most long-standing disease of significance in this patient, I am sure, was gallstones. We found a large stone in the cystic duct, another large one in the common duct, and many smaller ones in the dilated intrahepatic bile passages. The gall bladder was shrunken and shriveled, but was not perforated. We also found a

series of abscesses, one of which was in the pelvis in the general region where the peritoneoscopist had noticed adhesions of the small bowel. Another was beneath the right lobe of the diaphragm, and a third around the spleen beneath the left lobe of the diaphragm. The abscess on the right had perforated through the diaphragm and into the lung. There was also a large abscess within the liver. The peritoneal cavity was free from generalized peritonitis, but there were a number of small yellow spots that had been noted by the peritoneoscopist and described as flecks of fibrin. On incision they were found to contain fluid. On careful examination of that fluid and also of the fluid in the many abscesses, multiple sulfur granules were grossly evident—in other words, actinomycosis. There were no pulmonary emboli, and we have no anatomic explanation of the two episodes of collapse. They may have been associated with sudden extensions

of the infection, such as rupture of the liver abscess into the subdiaphragmatic space and extension through the diaphragm. Among many other anatomic landmarks, this patient had double pelvis and ureters in both kidneys, a rather large adenomatous hyperplasia of one adrenal gland, fibroids of the uterus, multiple small neurofibromas of the stomach, some healed pulmonary tuberculosis and generalized diverticulosis of the sigmoid colon.

DR. ALLEN: What was the mass displacing the stomach? Was that an abscess?

DR. MALLORY: That was an abscess, mostly intrahepatic, not perihepatic.

DR. ALLEN: I recall one patient who had a perforation of the diaphragm following a subdiaphragmatic abscess associated with perforated duodenal ulcer and who went into collapse and died in a manner not unlike this one in about the same number of hours.

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## THE STAFF OF LIFE

THE United States, according to the June *News Letter* of the Department of Agriculture, is failing to meet its commitments in the export of foods to famine-stricken countries. We failed to meet our goal for both grain and fats and oils during the first quarter of the year and that for grain in April, and the 80 per cent flour-extraction program will save only 15 to 20 million bushels of wheat instead of the 25 million expected. The 30-cent bonus per bushel offered for wheat delivered before May 25 has, however, encouraged farmers to make their stocks available, and wheat has begun to move. Still, to accomplish our aims, the production of flour for domes-

tic use must be cut to 75 per cent of the May and June distribution of last year. Distillers have already been limited to three days' operation a month, and the use of grain in feeding livestock has been drastically cut. For the first time in our history, bread has literally assumed its allegorical importance and has become the staff of life.

Whether productive countries and countries whose economic affairs are conducted on a reasonably progressive plane should attempt the obviously impossible task of feeding those whose population increases are far beyond their capacities to support is a debatable matter. The question of tiding our usually self-supporting neighbors over a period of famine caused by such unnatural circumstances as a world war is something else, we are bound to a special type of obligation. And yet it seems to be a fact that, despite all publicity up to the present time, the people of this country are confused regarding their obligations, are uninformed on the sacrifices necessary to discharge them and have found, unfortunately, no reason for believing that their guides in these important matters are themselves particularly well informed.

During the war, when general food rationing was in effect, many of us frequently knew about where we stood on the problem of balancing our diets, we were bound to a common cause and knew what to expect in the performance of our tasks. Now, in the peace that literally passeth all understanding, we are beset by more difficulties than we encountered during the war, except that of the war itself.

Good leadership, in an enlightened country, should be a leadership that further enlightens those who are willing and need to be led. We are disturbed, not because we want more than we are getting, but because we want to know the reasons why certain things are lacking, and we want those reasons to be good. We want to know why meat is scarce, and if it is because 90 per cent is going into the black market, we want to have something done about it.

During the past years when butter became difficult to obtain because of our large armed forces, we used oleomargarine and liked it. Now that we can get neither butter nor oleomargarine, we are troubled because we are afraid that bread is being withdrawn so that we shall not miss the butter that

we cannot get to put on it. We are willing to play along with the Magi, but we should like to know that they know the answers, and that the answers do not change too often.

### THE CHANGING POTENCY OF COMMERCIAL PENICILLIN

MANY physicians who have been using penicillin in the treatment of serious infections have become aware of the increasing doses required to accomplish the therapeutic results that they have become accustomed to expect. This has been compensated for, in part, by the greater availability of the product and by an increase in its purity, the latter having made possible the injection of large numbers of units in small volumes, with a decrease in the amount of irritation experienced from the injections. The decline in the effectiveness of commercial penicillin has been statistically quantitated so far as the treatment of syphilis is concerned, and it has been shown that the results of penicillin treatment of early syphilis have been distinctly less satisfactory since May, 1944, than prior to that date.<sup>1</sup> The reason for this change has been shown unmistakably to be an alteration in the character of the commercial preparations of penicillin.<sup>2</sup> Recent products have also been found to be less effective in the treatment of experimental pneumococcal and streptococcal infections.<sup>3</sup>

It is known that commercial penicillin contains at least four molecular species identified as F, G, K, and X, which differ from each other only in the nature of the side group attached to a common nuclear structure.<sup>4</sup> These forms of penicillin vary significantly in their antibacterial activity in vitro. Until recently therapeutic activity has been found in general to parallel in-vitro activity. Eagle and Musselman<sup>3</sup> discovered, however, that the activity of penicillin K in experimental infections of animals did not parallel the activity of this species of penicillin in vitro. The basis for this discrepancy was the rapid drop in blood levels and the small urinary recoveries after a given dose of penicillin K, as compared with that of penicillin G, at any time after an injection of a specified amount of various forms of penicillin, the levels of penicillin K were much lower than those observed with the other

penicillins, and penicillin K persisted at any given level for much shorter periods. In both rabbits and man the recovery of penicillin K in the urine averaged 30 to 35 per cent. This compares with an average recovery for penicillins F, G and X of 74 per cent in rabbits and 91 per cent in man.

In pneumococcal infections of mice an impure preparation of penicillin K was one-sixth as active as penicillin G (the form that formerly predominated in commercial penicillins) and one-eighth as active as penicillin X. In the treatment of experimental streptococcal infections in mice a pure preparation of penicillin K was one-eleventh as active as penicillin G and one-thirtieth as active as penicillin X. In experimental syphilis in rabbits penicillin K was found to be about one-tenth as effective as penicillin G. These findings suggest that penicillin K is inactivated in the body to a greater extent and more rapidly than are the other forms of penicillin and thus gives a lower therapeutic activity than would be anticipated from its bactericidal action in vitro.

Unfortunately, preparations of penicillin being supplied currently by the majority of the large producers have shown an increasing proportion of penicillin K. Since the number of units represents only the results of titrations in vitro against a single strain of staphylococcus, it is not possible to predict either the proportion of penicillin K or the amount of therapeutic activity that is present in any of these preparations. It seems clear that the amounts of penicillin K in commercial penicillin should be minimized, and it also seems desirable to standardize impure mixtures of penicillin for therapeutic use by some method other than the bactericidal activity in vitro. Until such a method is devised, it is essential to use considerably larger doses of penicillin in the therapy of infections than were formerly considered effective.

### REFERENCES

1. Committee on Medical Research and the United States Public Health Service. Treatment of early syphilis with penicillin. *J A M A* 131:265-271, 1946.
2. Committee on Medical Research. The United States Health Service and The Food and Drug Administration. Changing character of commercial penicillin with suggestions as to use of penicillin in syphilis. *J A M A* 131:271-275, 1946.
3. Eagle, H. and Musselman, A. Low therapeutic activity of penicillin K relative to that of penicillins F, G and X, and its pharmacological basis. *Science* 103:618-620, 1946.
4. Committee on Medical Research, O S R D. Washington, and the Medical Research Council, London. Chemistry of Penicillin. *Science* 102:627-629, 1945.

## NEW HAMPSHIRE MEDICAL SOCIETY

### DEATH

SANDERS — Loren A. Sanders, M.D., of Concord, died April 24. He was in his seventy-second year.

Dr. Sanders received his degree from the New York University College of Medicine in 1899. He was medical referee for Merrimack County and attending surgeon at the New Hampshire Memorial Hospital. He was a fellow of the American College of Surgeons.

His widow survives.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### LIST OF MASSACHUSETTS LABORATORIES HOLDING CERTIFICATES OF APPROVAL

The Department of Public Health has just published its first list of the laboratories in the Commonwealth currently holding certificates of approval, indicating the tests for which each laboratory is approved. Copies have been mailed to all hospital superintendents and chiefs of staff, as well as to the laboratory directors and head technicians of the approved laboratories themselves.

The approval of bacteriologic and serologic laboratories stems from Section 184A of Chapter 111, which was passed in 1939, stating that the Department may at the request of a laboratory issue a certificate of approval for the performance of designated bacteriologic and serologic tests that the Department finds the laboratory capable of performing satisfactorily. Application is voluntary, but laboratories are urged to seek approval for all tests that they routinely perform, not for those done elsewhere.

The approval of a laboratory is determined essentially by the qualifications of its personnel, the suitability of its quarters and equipment, the use of accepted methods, the satisfactory performance of its work and the maintenance of adequate laboratory records. Accuracy of tests is ascertained by ability to maintain close agreement with other laboratories on specimens sent out periodically to approved laboratories by the State Bacteriological and Wassermann laboratories. This is the most important single method for evaluation of a laboratory. From time to time visits are made by a member of the Department to reappraise the laboratory and to make suggestions when desired. A certificate of approval is granted for one year, and renewal is dependent on a continued satisfactory standard.

Chapter 155 of the Acts of 1946 extends the laboratory-approval program to include ordinary blood grouping and Rh blood testing, as well as cross matching of donors and recipients for blood transfusions. In addition, it authorizes the issuance of

certificates of approval for laboratory tests on milk, foods, eating utensils, water and sewage. A list of laboratories approved for these additional tests will be available later.

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS UNDER THE PROVISIONS OF THE SOCIAL SECURITY ACT

CLINIC	DATE	CLINIC CONSULTANT
Haverhill	July 3	William T. Green
Gardner	July 9	John W. O'Meara
(Worcester Sub-clinic)		
Brockton	July 11	George W. Van Gorder
Pittsfield	July 15	Frank A. Slowick
Salem	July 15	Paul W. Hugenberger
Worcester	July 19	John W. O'Meara
Fall River	July 22	David S. Grace
Hyannis	July 23	Paul L. Norton

Physicians referring new patients to clinic should get in touch with the District Health Officer to make appointments.

### MISCELLANY

#### CONSULTATION SERVICE FOR DIAGNOSIS AND TREATMENT OF MALIGNANT TUMORS OF IN- FANCY AND CHILDHOOD

Announcement is made of the establishment of a consultation service to provide assistance in the diagnosis and treatment of tumors of infancy and childhood. This is a further step in the organization of the Children's Cancer Center, a unit of the Medical Center for Children in Boston.

This is not a tumor registry. It is designed, rather, to give without charge immediate diagnostic assistance and advice concerning therapy and prognosis to any doctor who will send the necessary clinical data, microscopic sections and x-ray films. Replies will be given by air mail or, when necessary, by telephone or telegraph. The project, which is supported in part by a grant-in-aid from the National Advisory Cancer Council, will be paralleled by a research program concerning the biology of tumors of early life, together with a consideration of the clinical, pathological and epidemiologic aspects of the problem.

The consultation service will be rendered by a group of three pathologists, Dr. S. Burt Wolbach, Dr. Charles F. Branch and Dr. Sidney Farber, and one roentgenologist, Dr. Edward D. B. Neuhauser, with the co-operation, when indicated, of the entire staff of the Children's Hospital, through the chiefs of the clinical services. Doctors representing all the clinical and laboratory specialties concerned with the infant or child will be available for consultation.

Communications should be sent to Dr. Sidney Farber, Children's Hospital, 300 Longwood Avenue, Boston 15, Massachusetts. The service will begin to function on August first.

### CORRESPONDENCE

#### AMERICAN COMMITTEE FOR YUGOSLAV RELIEF

To the Editor: We medical men know that the work of saving human lives knows no boundaries. The horror of war is over, but the battle for survival is still going on in Yugoslavia. It must be said that disease and death conquer even where the Nazis failed.

During the war, Yugoslavia lost nearly 2,000,000 — 15 per cent of the total population. We make a plea for the living, many of whom are also doomed to die unless you help them. We speak for the 1,487,000 children in desperate need of medical care. We speak for 150,000 known victims of tuberculosis. We speak for 1,000,000 persons infected with malaria. We appeal for their very lives.

Statistics all too frequently dull the imagination, yet we cannot present the medical case of Yugoslavia without them. Please bear in mind that figures denote people and people are suffering. In Macedonia half the population has malaria. In Yugoslavia as a whole, 1 out of 25 has tuberculosis and the death rate from tuberculosis is ten times higher than that in the United States. In prewar Yugoslavia the infant mortality rate was the highest in Europe, with 155 dead for every 1000 living births, as compared with 56 in the United States. Now the infant mortality rate has risen to 170, while in Greater New York it has decreased to 35, in Sweden to 30 and in England to 38.

As against this background of widespread disease and soaring death rates, consider the medical facilities now available to the Yugoslavs. In all of Yugoslavia there are but 12,000 hospital beds. For the 150,000 people with active tuberculosis who require hospitalization, there are only 1500 beds. In mountainous Yugoslavia with its shattered communications there is but 1 doctor to every 5000 people, and in isolated communities it is nearer 1 doctor to every 10,000—Greater New York has 1 physician to 450 persons. Tuberculosis-ridden Yugoslavia has but 2 chest surgeons. These are the figures.

Yugoslavia needs—desperately needs—hospitals, clinics, research laboratories and facilities for training doctors and nurses. The American Committee for Yugoslav Relief, 235 East 11th Street, New York City, is conducting a campaign for \$5,000,000 to provide some part of these medical necessities. We feel sure that the health program of the Committee will meet with warm response. Our land is rich, the will of the people to help, unprecedented, and its generosity, unsurpassed.

BÉLA SCHICK, M.D.  
KENDALL ENERSON, M.D.  
EVA D. THOMAS, M.D.  
ZHIVKO ANGELUSCHEFF, M.D.

235 East 11th Street  
New York 3, New York

## BOOK REVIEWS

*The History of Surgical Anesthesia*. By Thomas E. Keys, M.A. With an introductory essay by Chauncey D. Leake, and a concluding chapter, "The Future of Anesthesia," by Noel A. Gillespie. 8°, cloth, 191 pp., with 43 illustrations. New York: Schuman's, 1945. \$6.00.

This authentic and official history of anesthesia represents a synthesis of five essays and a chronology of anesthesia previously published by the author, well known as reference librarian for the Mayo Clinic. The introductory essay by Professor Leake, of the University of Texas, who developed the use of divinyl oxide, discusses the nature of pain and anesthesia and the discovery of modern anesthetic agents. The body of the text by Major Keys presents a complete history of the development of anesthesia, followed by a chronology of events relating to anesthesiology and allied subjects, with a bibliography of over three hundred references arranged both by subject and by author. Dr. Gillespie's concluding chapter forecasts the further development of the professional anesthetist as a specialist in medicine. An appendix by Dr. John F. Fulton of Yale University, contains his bibliographic study of the Morton and Warren letheon tracts. This authoritative and scholarly work of reference is admirably illustrated by an engraved frontispiece and by forty-five well selected text figures.

*Radiologic Examination of the Small Intestine*. By Ross Golden, M.D. 4°, cloth, 239 pp., with 75 illustrations. Philadelphia: J. B. Lippincott Company, 1945. \$6.00.

This is an excellent monograph by a highly qualified author on a much neglected portion of the human anatomy. It is the ideal prescription for the manuscripts desired by all medical-book publishers, and it is truly fulfilled in this 200-page book, profusely and well illustrated. It matters little that the so-called "deficiency states," mesenteric lesions, hypoproteinemia and other conditions all present a similar x-ray pattern. The chief value of this book is that it focuses

attention on disorders of motor function in the small bowel and details methods of study and analysis that may result in definite clinical dividends, as well as the accumulation of factual physiologic data.

There are excellent chapters on the anatomy and physiology of the small bowel, on the use of the Miller-Abbott tube and on all the various pathologic processes that may involve this clinical terra incognita.

This monograph is a great credit to the author and should be a source of pride to the publishers, as it is well and accurately put together. Of interest and value chiefly to radiologists, it should be owned and carefully studied by all physicians who try to diagnose or treat gastrointestinal disease.

## BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

*The Fundamentals of Electrocardiographic Interpretation*. By J. Bailey Carter, M.D., assistant (Rush) professor, Department of Medicine, University of Illinois College of Medicine and member of attending staff, Cook County and Augustana hospitals, Chicago. With a foreword by Horatio B. Williams, M.D., Dalton Professor of Physiology, College of Physicians and Surgeons, Columbia University, New York. Second edition. 8°, cloth, 406 pp., with 307 illustrations. Springfield, Illinois: Charles C. Thomas, 1945. \$6.00.

This second edition of a manual first published in 1937 has been thoroughly revised and brought up to date. The book is not a report of research, and debatable questions have been avoided. The manual is designed to aid the beginner in acquiring a practical working knowledge of the subject. Much of the material concerning coronary disease is new or has been rewritten. Many new illustrations have been added, and the extensive bibliographies appended to each chapter have been brought up to date.

*Common Ailments of Man*. Edited by Morris Fishbein, M.D. 8°, cloth, 177 pp., illustrated. Garden City: Garden City Publishing Company, Incorporated, 1945. \$1.00.

This popular manual has been designed to further the layman's knowledge of the ills that are likely to beset him. The various articles on common ailments by recognized medical specialists have been reprinted from *Hysgia*.

*Penicillin and Other Antibiotic Agents*. By Wallace E. Herrell, M.D., M.S., assistant professor of medicine, Mayo Foundation, University of Minnesota, and consultant in medicine, Mayo Clinic, Rochester, Minnesota. 8°, cloth, 348 pp., with 45 illustrations and 45 tables. Philadelphia: W. B. Saunders Company, 1945. \$5.00.

In this monograph Dr. Herrell has tried to bring together the fundamental, experimental and clinical studies that have been carried on with penicillin and other antibiotic agents. The book is divided into four parts. The first has to do with the history, preparation and chemistry of penicillin. The second and third, comprising the major portion of the text, concerns the clinical use of penicillin. The fourth discusses other antibiotic agents, including tyrothricin, streptothricin, streptomycin and other miscellaneous agents.

*Physical Diagnosis*. By Ralph H. Major, M.D., professor of medicine, University of Kansas. Third edition revised. 8°, cloth, 444 pp., with 458 illustrations. Philadelphia: W. B. Saunders Company, 1945. \$5.00.

This third edition of a standard text has been revised in the light of recent advances since the publication of the second edition in 1940.

*Principles of Psychology for the Basic Course in Nursing*  
By Rev J Edward Rauth, O S B, Ph D, and Sister M Maurice Sheehy, R S M, R N, Ph D, assistant professor of nursing education, Catholic University of America 12<sup>o</sup>, cloth, 200 pp, with 18 illustrations and 8 tables Milwaukee The Bruce Publishing Company, 1945 \$2.00

This small manual is based on the authors' experience in teaching psychology in schools of nursing. It is designed as a teaching manual, and the applications of psychological principles of various nursing situations have been indicated in the text and a few case histories have been included. This text is not a book for self-study but is intended to be used as a basis for discussion with the teacher.

*Bronchial Asthma* By Leon Unger, M.D., assistant professor, Department of Medicine, Northwestern University Medical School, Chicago. With an introduction by Morris Fishbein, M.D., editor, *Journal of the American Medical Association* 8<sup>o</sup>, cloth, 724 pp, with 126 figures Springfield, Illinois Charles C Thomas, 1945 \$9.00

This work on bronchial asthma has been written from the viewpoint of allergy, and the author has endeavored to present a comprehensive treatise on his subject. Extended discussion is given to etiology, including constitutional and exciting factors. The exciting factors are divided into inhalants (allergens), ingestants (foods and drugs) and miscellaneous (silk, parasites, physical agents and bacteria). The author believes that the most important causes of asthma are the inhalants or allergens, and these substances are described in considerable detail. Following are extensive chapters on diagnosis, symptomatology, pathology and treatment (specific and nonspecific), including the sources of allergens, elimination diets, patent medicines used in asthma, and physical exercises for asthmatics. The laboratory section describes the preparation of extracts. There are chapters on other allergic diseases related to asthma and on the military aspects of the disease. The beginning chapters consider the technical terms used and their interpretation, as well as the history of bronchial asthma from ancient times to the present. Selected references are appended to each chapter and the printing is well done, with a good type on good paper. Dr Morris Fishbein in his introduction characterizes the work as the most complete consideration of the subject thus far available in any single book.

## NOTICES

### FELLOWSHIPS FOR THE STUDY OF RHEUMATIC FEVER

The American Council on Rheumatic Fever of the American Heart Association announces that applications for American Legion fellowships for the study of rheumatic fever will be accepted from recognized institutions concerned with the study of rheumatic fever and rheumatic heart disease. Two fellowships are available, each is for a period of three years and carries a stipend of \$3500, \$4000 and \$5000 for the first, second and third years respectively.

Each application should supply information concerning the institution, the projected study and the individual proposed for the fellowship. Applications will be received until August 1, 1946, and will become effective September 1, 1946.

These fellowships have been made available by a grant from the American Legion and the Women's Auxiliary of the American Legion as part of their program of fostering research in rheumatic fever and rheumatic heart disease.

### INDUSTRIAL HEALTH CONGRESS

The seventh Annual Congress on Industrial Health will be held in Boston September 30 through October 3 at the Copley-Plaza Hotel, under the sponsorship of the Council on Industrial Health of the American Medical Association.

The program, as in the past, will include speakers of national note and is expected to attract hundreds of medical men, nurses, hygienists and, in addition, legislators, industrialists and others interested in the field of health in industry.

At a later date further announcements relative to the exact program will be made in the *Journal*. Because of the importance of the meeting, those expecting to attend are urged to make their hotel and transportation plans as early as possible.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Tuesday, July 9, at 11:00 a.m. in the classroom of the Nurses' Residence. Dr Edwin B. Astwood will speak on the subject "Thiouracil in the Treatment of Hyperthyroidism." Dr Merry Pittman will be chairman.

### ANNOUNCEMENTS

Dr Franklin G. Balch, Jr., has returned from naval duty and will resume the practice of surgery at 330 Dartmouth Street, Boston.

Dr Francis F. Cary announces the opening of an office for the practice of internal medicine in the Professional Building, 58 Federal Street, Greenfield.

Dr James Harrison announces his return from military service and the reopening of his office for the practice of medicine at 69 Bridge Street, Dedham.

Dr A. Macaluso, having been released from active service in the U. S. Naval Reserve, announces his return to practice with an office at 484 Commonwealth Avenue, Boston.

### SOCIETY MEETINGS AND CONFERENCES

#### CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 4

- FRIDAY, JULY 5**  
\*10:00 a.m.-12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.
- TUESDAY, JULY 9**  
12:00 m.-1:00 p.m. Dermatological Service, Grand Rounds. Amphitheater, Dowling Building. Boston City Hospital.  
\*12:15-1:15 p.m. Chnicroentgenological Conference. Peter Bent Brigham Hospital.
- WEDNESDAY, JULY 10**  
\*10:30-11:30 a.m. Medical Clinic. Isolation Building Amphitheater, Children's Hospital.  
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\*2:30-4:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

\*Open to the medical profession.

- MARCH 15-SEPTEMBER 15. Boston University Course for Discharged Medical Officers. Page 240. Issue of February 14.
- JUNE 29. American College of Chest Physicians. Page 544, issue of April 18.
- JULY 3. Harvard Medical Alumni Association. Page 808, issue of June 13.
- JULY 9. New England Hospital for Women and Children. Notice above.
- SEPTEMBER 4-7. American Congress of Physical Medicine. Page 616, issue of May 2.
- SEPTEMBER 30-OCTOBER 3. Industrial Health Congress. Notice above.
- OCTOBER 6-12. Interamerican Congress of Cardiology. Page xix, issue of June 6.
- OCTOBER 7-18. New York Academy of Medicine. Page 544. Issue of April 18.

### DISTRICT MEDICAL SOCIETY

#### PLYMOUTH

- OCTOBER. Jordan Hospital, Plymouth.
- NOVEMBER. Plymouth County Hospital, South Hanson.
- JANUARY. Brockton Hospital, Brockton.
- FEBRUARY. Moore Hospital, Brockton.
- MARCH. Goddard Hospital, Brockton.
- APRIL. State Farm, Bridgewater.
- MAY. Lakeville Sanatorium, Lakeville.





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